☐ 1: Arthritis Rheum. 1993 Feb;36(2):234-42.



# Increased production of soluble CD23 in rheumatoid arthritis, a its regulation by interleukin-4.

**Chomarat P, Briolay J, Banchereau J, Miossec P.**

Schering-Plough Laboratory for Immunological Research, Dardilly, France.

OBJECTIVE. To assess CD23 status in rheumatoid arthritis (RA) patients, a defined by the levels of CD23 expression on peripheral blood mononuclear c (PBMC), the levels of soluble CD23 (sCD23) in sera, and the production of sCD23 by PBMC cultures and its regulation by interleukin-4 (IL-4). METHODS. CD23 expression as determined by double fluorescence-activat cell sorter analysis and sCD23 production as determined by immunoradiome assay were investigated in 24 RA patients and 21 controls. Soluble CD23 wa measured in sera and supernatants of PBMC, activated with polyclonal activators (pokeweed mitogen [PWM] or Staphylococcus aureus Cowan strai [SAC]) used either alone or in combination with IL-2 or IL-4. RESULTS. Th percentage of B cells expressing CD23 and serum levels of sCD23 were increased in patients with RA. IL-4 was a potent inducer of sCD23 productio supernatants, whereas IL-2 was inactive. Costimulation with SAC or PWM d not increase the effect obtained with IL-4 alone. When sCD23 levels in RA a control supernatants were compared, spontaneous production was found to b increased in RA PBMC. This difference from control values was even more pronounced when sCD23 levels in PBMC and purified B cells in response to 4, either alone or in combination with SAC or PWM, were tested. In the sam supernatants, the increased secretion of sCD23 induced by IL-4 was associat with an inhibitory effect of IL-4 on Ig production, a phenomenon that was m pronounced in RA PBMC than in controls. CONCLUSION. CD23 status in I is characterized by increased expression of CD23 on B cells, increased production of sCD23 in sera and supernatants, and increased sensitivity of R PBMC and B cells to IL-4.

PMID: 8431213 [PubMed - indexed for MEDLINE]

1: J Clin Immunol. 1999 Jul;19(4):215-22.





# The importance of specific IgG and IgE autoantibodies to retina antigen, total serum IgE, and sCD23 levels in autoimmune and infectious uveitis.

**Muino JC, Juarez CP, Luna JD, Castro CC, Wolff EG, Ferrero M, Romero-Piffiguer MD.**

Allergy and Immunology Section, Internal Medicine Service, Misericordia Hospital, Cordoba, Argentina.

Autoimmunity plays an important role in the development of uveitis. The uv are linked to Th1 or Th2 lymphocyte activation. We studied 41 patients with uveitis, divided into autoimmune uveitis (n = 32) and infectious uveitis (n = 30 normal controls, and 20 asthmatic atopic without ocular diseases. The infectious uveitis patients were separated into bacterial (n = 6) and toxoplasn (n = 3) retinochoroiditis. We measured IgE and sCD23 serum levels and spec IgG and IgE to retinal S antigen by ELISA tests. The IgE levels were 500 +/- 325 kU/L in autoimmune uveitis, 57 +/- 35 kU/L in bacterial uveitis, 280 +/- kU/L in toxoplasmic retinochoroiditis, 75 +/- 32 kU/L in the controls, and 55 +/- 243 kU/L in atopics ($P < 0.0005$). The sCD23 levels were 10.4 +/- 5.4 ng in autoimmune uveitis, 3.7 +/- 1.17 ng/ml in bacterial uveitis, 6.76 +/- 1.36 ng/ml in toxoplasmic retinochoroiditis, 3.4 +/- 1 ng/ml in controls, and 8.35 - 2.2 ng/ml in atopic patients ($P < 0.005$). The specific IgG to retinal S antigen was positive in 27 of 32 cases, and the specific IgE to retinal S antigen was positive in 22 of 32 autoimmune uveitis. The bacterial uveitis patients as wel the controls were negative for both autoantibodies to retinal S antigen. The toxoplasmic retinochoroiditis patients presented specific IgG and IgE to retin antigen in two of three cases, respectively, one of them with overlap of both antibodies. These results suggest the importance of specific IgG and IgE to retinal S antigen in autoimmune uveitis, which, along with higher IgE and sCD23 levels, reveal Th2 activation.

PMID: 10471975 [PubMed - indexed for MEDLINE]

1: Scand J Immunol. 1999 Jan;49(1):78-81.



# CD23 antigen expression on B lymphocytes and soluble CD23 levels in peripheral blood of high-risk type 1 diabetes subjects.

**Kretowski A, Szelachowska M, Pietruczuk M, Kinalska I.**

Department of Endocrinology, Medical School Bialystok, Poland.

Soluble CD23 (sCD23), a recently discovered multifunctional cytokine, is a 
kDa molecule released by autoproteolysis from the 45-kDa CD23 molecule which is found mainly on the surface of B lymphocytes. In the present study aimed to evaluate, in association with humoral immune and metabolic marke the changes in CD23 antigen expression on B lymphocytes and levels of sCI in the peripheral blood of subjects at high risk of type 1 diabetes. The study v carried out in 28 first-degree relatives of type 1 diabetes patients (versus a control group of 28 age- and sex-matched healthy volunteers) using antibodi against different B-cell antigens: ICA, GADA, IAA, IA-2. Flow cytometry w used to measure the percentage of CD20+ (B lymphocytes) and CD20+CD2 lymphocyte subsets, and sCD23 levels in serum were determined by enzyme immunoassay. Prediabetic subjects had a significantly ($P<0.01$) lower percentage of CD20+CD23+ lymphocytes in comparison with healthy age- a sex-matched controls. Expression of CD23+ on B lymphocytes was similar i subjects with ICA only and with two or more antibodies against pancreatic antigens. In the prediabetic group, the median concentration of sCD23 was l than in the control group and was statistically significant ($P < 0.02$) in the subgroup of subjects with the most impaired function of pancreatic beta-cells (the lowest values of first phase of insulin release). In conclusion, our study suggests that CD23 molecule expression on B lymphocytes and sCD23 level peripheral blood could be additional markers for monitoring the developmen type 1 diabetes and play a role in determining the efficacy of prevention trial However, further prospective studies are needed.

PMID: 10023861 [PubMed - indexed for MEDLINE]

1: Diabet Med. 1998 Apr;15(4):320-6.



# Enhancement of soluble CD23 serum levels and cell-surface CD2 expression in subjects at increased risk of type 1 diabetes mellitu and in diabetic patients.

**Avanzini MA, Vitali L, d'Annunzio G, De Amici M, Strigazzi C, Alibran A, Lorini R.**

Laboratori Sperimentali di Ricerca, IRCCS, Policlinico S. Matteo, Pavia, Ital

The low affinity receptor for IgE, CD23, is expressed on lymphocytes among other cell types. The purpose of the present study was to assess serum sCD23 levels and CD23 expression on peripheral blood mononuclear cells (PBMC) people at increased risk of developing Type 1 diabetes mellitus and in diabet patients. Serum sCD23 levels were significantly higher in first-degree relativ of Type 1 patients (median: 3.2 U ml(-1)) ($p < 0.001$) and in newly diagnose (median: 3.3 U ml(-1)) ($p < 0.001$) and long-standing (median: 2.5 U ml(-1)) = 0.01) Type 1 diabetic patients than in controls (median: 1.2 U ml(-1)). New diagnosed patients showed higher levels than those with long-standing diseas = 0.026). Moreover the percentage of B cells expressing CD23 were significantly higher in first-degree relatives (median: 48.6%) ($p < 0.001$) and newly diagnosed (median: 58%) ($p < 0.001$) and long-standing (median: 44.8 ($p = 0.03$) Type 1 diabetic patients than in controls (median: 28.5%). The increased sCD23 levels and the increased number of cells expressing CD23 observed in subjects at increased risk of Type 1 diabetes and diabetic patients may be indicators of Th2 activity in Type 1 diabetes.

PMID: 9585398 [PubMed - indexed for MEDLINE]

1: J Neuroimmunol. 1995 Aug;61(1):1-5.

Related Articles,

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# In vitro cytokine, sCD23 and IgG secretion in multiple sclerosis.

**Zaffaroni M, Stampino LG, Ghezzi A, Baldini SM, Zibetti A.**

Centro Studi Sclerosi Multipla, University of Milano, Hospital of Gallarate, Italy.

Synthesis of IgG by peripheral blood mononuclear cells from patients with multiple sclerosis (MS) and with other neurological diseases and from health controls was induced by Pokeweed mitogen (PWM) in short-term cultures. A expected, MS patients produced more immunoglobulin (Ig) G and had a high percentage of 'high responders' to PWM stimulation as compared to controls. Interleukin (IL)-4 was undetectable in all samples. IL-6 and tumor necrosis factor (TNF)-alpha synthesis was induced by PWM stimulation in all groups. MS patients showed the most significant increase of both cytokines. Interestingly, only MS patients showed a significant increase of the soluble f of CD23 receptor (sCD23). Moreover, only sCD23 levels correlated with in IgG production in MS patients. The levels of IL-6, TNF-alpha, sCD23 were greater in high responders compared to low responders in all groups. The me value of each molecule, however, did not differ significantly among overall groups. A highly significant difference was reported for sCD23 in MS patien We suggest that sCD23, also known as B cell growth factor, may play a role the well-documented phenomenon of in vitro IgG hypersynthesis in MS pati adding support to the concept of B cell up-regulation in the peripheral blood these patients.

PMID: 7560007 [PubMed - indexed for MEDLINE]

☐ 1: J Neuroimmunol. 1994 Dec;55(2):127-33.

Related Articles,

# Expression of Fc epsilon R2/CD23 and p55 IL-2R/CD25 on peripheral blood macrophages/monocytes in multiple sclerosis.

**Tsukada N, Miyagi K, Matsuda M, Yanagisawa N.**

Department of Health Medical Center and Neurology, Shinshu University, Matsumoto, Japan.

Macrophages have been found histologically to be activated in multiple sclerosis. We analyzed the expression of CD23 and CD25 on monocytes/macrophages in peripheral blood obtained from patients with multiple sclerosis (MS) to investigate their role in the demyelinating process. Peripheral blood mononuclear cells were obtained from 30 patients with MS including four BalÃ³'s diseases (24 with acute relapsing type disease, six witl chronic progressive type disease) and 12 healthy controls. The percentage of CD14+CD23+ monocytes/macrophages and CD14+CD25+ monocytes/macrophages were determined by two-color flow cytometry. The percentage of CD14+CD23+ monocytes was significantly higher in patients MS in the active phase as compared with controls ($P < 0.01$). Six patients wit acute relapsing MS, who had received no therapy, had higher CD14+CD23+ cells than did controls ($P < 0.0001$). CD14+CD25+ monocytes/macrophages were not detected in peripheral blood monocytes/macrophages of patients wi MS except BalÃ³'s concentric sclerosis. The four patients with BalÃ³'s concentric sclerosis had markedly elevated levels of CD14+CD25+ monocytes/macrophages. Our findings suggest that monocytes/macrophages activated during an exacerbation of MS, and that they may play an important role in the process of demyelination.

PMID: 7530259 [PubMed - indexed for MEDLINE]

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☐ 1: J Dermatol Sci. 2004 Jun;35(1):53-9.

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# Elevated expression of CD23 on peripheral blood B lymphocytes from patients with bullous pemphigoid: correlation with increas serum IgE.

**Inaoki M, Sato S, Takehara K.**

Department of Dermatology, Kanazawa University Graduate School of Medi Science, 13-1 Takara-machi, Kanazawa 920-8641, Japan. inaoki-m@med.kawasakim.ac.jp

BACKGROUND: Increased serum IgE levels are occasionally found in patie with severe bullous pemphigoid (BP). CD23, a low affinity Fc receptor for Ig is mainly expressed on mature B lymphocytes. Studies have suggested that serum levels of soluble CD23 (sCD23) correlate with serum IgE levels and disease severity in BP. OBJECTIVE: The purpose of our study is to examine whether the expression of CD23 is elevated in BP and whether this expressio correlates with serum IgE levels and disease severity. METHODS: We meas CD23 expression on B cells from patients with active BP, pemphigus vulgari pemphigus foliaceus, and atopic dermatitis (AD), as well as healthy control subjects, using a flow cytometer. Serum levels of IgE and sCD23 were also measured. RESULTS: The expression of CD23 was significantly higher in B patients compared with healthy control subjects ($P < 0.05$), whereas the level were normal in the other bullous diseases. CD23 expression tended to be hig in severe BP compared with moderate BP, and the levels in severe BP were comparable to the levels in AD. Furthermore, CD23 expression correlated positively with serum IgE levels ($P < 0.002$), and the IgE levels were significantly higher in severe BP than in moderate BP ($P < 0.01$ ). CD23 expression in BP did not correlate with sCD23 levels. CONCLUSIONS: The results suggest that the up-regulated surface CD23 on B cells may be involve IgE synthesis and inflammatory events in BP. Copyright 2004 Japanese Soci for Investigative Dermatology

PMID: 15194147 [PubMed - in process]

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1: Nat Med. 1995 Aug;1(8):781-5.



# Marked amelioration of established collagen-induced arthritis b treatment with antibodies to CD23 in vivo.

**Plater-Zyberk C, Bonnefoy JY.**

Glaxo Institute for Molecular Biology, Immunology Department, Geneva, Switzerland.

CD23 is a low-affinity receptor for immunoglobulin E (IgE) expressed by a variety of haematopoietic cells. Proteolytic cleavage of the transmembrane receptor generates soluble forms, which can be detected in biological fluids. CD23 regulates many functional aspects of immune cells, both in its cell-associated and soluble forms. In view of the increased levels of CD23 in rheumatoid arthritis, we have studied the effect of neutralizing CD23 in type collagen-induced arthritis in mice, a model for human rheumatoid arthritis. Successful disease modulation is achieved by treatment of arthritic DBA/1 m with either polyclonal or monoclonal antibodies to mouse CD23. Treated mi show a dose-related amelioration of arthritis with significantly reduced clinic scores and number of affected paws. This improvement in clinical severity is confirmed by histological examination of the arthritic paws. A marked decre in cellular infiltration of the synovial sublining layer and limited destruction cartilage and bone is evident in animals treated with therapeutic doses of anti CD23 antibody. These findings demonstrate the involvement of CD23 in a mouse model of human rheumatoid arthritis.

PMID: 7585180 [PubMed - indexed for MEDLINE]

1: Eur J Immunol. 1990 Jan;20(1):139-44.

Related Articles,

# Inhibition of human interleukin 4-induced IgE synthesis by a subset of anti-CD23/Fc epsilon RII monoclonal antibodies.

**Bonnefoy JY, Shields J, Mermod JJ.**

Department of Cell Biology, Glaxo Institute for Molecular Biology, Geneva, Switzerland.

Specific monoclonal antibodies (mAb) directed against the CD23 antigen we used to study human interleukin 4 (hIL4)-induced IgE production by blood a tonsillar mononuclear cells. Both peripheral blood and tonsillar mononuclear cells stimulated by hIL4 expressed membrane CD23 as detected by the bindi of all anti-CD23 mAb. Nevertheless, two sets of anti-CD23 mAb could be distinguished. The first set, including mAb 25, was able to decrease significa hIL4-induced IgE synthesis by mononuclear cells. The second set, including EBVCS#1, did not affect hIL4-induced IgE synthesis. All the anti-CD23 mA were able to bind specifically to a human B cell line expressing recombinant CD23. Inhibition experiments revealed that the two sets of anti-CD23 mAb d not recognize the same epitope on the CD23 antigen. In fact, all the anti-CD2 mAb, except EBVCS#1, were able to inhibit IgE binding to CD23 on RPMI 8866 cells. Moreover, the first set of antibodies, which decreased IgE production, was able to up-regulate membrane CD23 expression on hIL4-stimulated tonsillar mononuclear cells. Conversely, EBVCS#1, which had nc effect on IgE production, did not affect hIL4-induced CD23 expression. Thes results indicate that CD23 plays a key role in human IgE synthesis.

PMID: 1689660 [PubMed - indexed for MEDLINE]

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☐ 1: J Immunol. 1994 Apr 15;152(8):3768-76.



# Induction of B cell and T cell tolerance in vivo by anti-CD23 mA

**Morris SC, Lees A, Holmes JM, Jeffries RD, Finkelman FD.**

Department of Medicine, Uniformed Services University of the Health Scien Bethesda, MD 20814.

T cell tolerance can be induced by B cell presentation of Ags to naive T cells further characterize this mechanism of T cell tolerance induction, we have investigated the effects of injecting mice with an intact rat IgG2a Ab, which binds to the B cell low-affinity Fc epsilon receptor (CD23), on the responsiveness of B cells and T cells to rat IgG2a. Our observations indicate 1) intravenous, subcutaneous, or intraperitoneal injection of this Ab induces antigen-specific B cell and T cell tolerance; 2) both forms of tolerance are induced more completely by injection of rat IgG2a anti-CD23 mAb than by injection of an equal dose of a control rat IgG2a Ig; and 3) reduced responsiveness to Ag is seen as early as 1 to 3 days after anti-CD23 mAb injection and reaches maximum levels by 7 days after injection. Although tolerance induced by the injection of soluble proteins has been reported to be characterized by reduced production of IL-2 and IFN-gamma, but normal production of IL-4, injection of mice with rat IgG2a anti-mouse CD23 mAb greatly decreases the IL-4 response to a rat IgG2a immunogen that normally induces a large IL-4 response.

PMID: 8144946 [PubMed - indexed for MEDLINE]

1: Science. 1993 Aug 20;261(5124):1038-41.



# Inhibition of an in vivo antigen-specific IgE response by antibod to CD23.

**Flores-Romo L, Shields J, Humbert Y, Graber P, Aubry JP, Gauchat JF Ayala G, Allet B, Chavez M, Bazin H.**

Glaxo Institute for Molecular Biology, Geneva, Switzerland.

Immunoglobulin E (IgE) mediates many allergic responses. CD23 is a 45-kilodalton type II transmembrane glycoprotein expressed in many cell types. a low-affinity IgE receptor and interacts specifically with CD21, thereby modulating IgE production by B lymphocytes in vitro. In an in vivo model o allergen-specific IgE response, administration of a rabbit polyclonal antibod recombinant human truncated CD23 resulted in up to 90 percent inhibition o ovalbumin-specific IgE synthesis. Both Fabs and intact IgG inhibited IgE production in vitro and in vivo. Thus, CD23 participates in the regulation of synthesis in vivo and so could be important in allergic disease.

PMID: 8351517 [PubMed - indexed for MEDLINE]

# Eosinophil IgE receptor and CD23.

**Capron M, Truong MJ, Aldebert D, Gruart V, Suemura M, Delespesse G Tourvieille B, Capron A.**

Centre d'Immunologie et de Biologie Parasitaire, Unite Mixte INSERM U16 CNRS 624, Institut Pasteur, Lille, France.

In the present review, eosinophil Fc epsilon RII was compared to CD23, a differentiation marker of B cells. Biochemical analysis revealed that molecul of similar molecular weight were immunoprecipitated from eosinophils and l cells by an anti-CD23 monoclonal antibody (mAb) or by BB10, and anti-eosinophil Fc epsilon RII. By flow cytometry, a correlation was found betwe the binding of anti-CD23 mAb and myeloma IgE. However, a low expressio different epitopes of CD23 was observed in various hypereosinophilic patien Northern blot analysis of eosinophil RNA with the cDNA probe of CD23 revealed a weak message in only 3 of the 6 patients expressing membrane CI The inhibition by anti-CD23 mAbs of IgE-mediated cytotoxicity and IgE binding to eosinophils clearly indicated the participation of CD23 or a relate molecule in IgE-dependent eosinophil functions. However, the differential effects of anti-CD23 mAbs on eosinophils and B cells suggest major differen in the characteristics of the molecule expressed by eosinophils and by B cells

Publication Types:

- Review
- Review, Tutorial

PMID: 1287119 [PubMed - indexed for MEDLINE]

1: Eur J Immunol. 1999 Sep;29(9):2957-67. Related Articles,



# Critical role of CD23 in allergen-induced bronchoconstriction in murine model of allergic asthma.

**Dasic G, Juillard P, Graber P, Herren S, Angell T, Knowles R, Bonnefoy JY, Kosco-Vilbois MH, Chvatchko Y.**

Department of Immunology Geneva Biomedical Research Institute, Glaxo Wellcome Research and Development S.A., Geneva, Switzerland.

CD23-deficient and anti-CD23 monoclonal antibody-treated mice were used investigate the role of the low-affinity receptor for IgE (CD23) in allergic air inflammation and airway hyperresponsiveness (AHR). While there were no significant differences in ovalbumin (OVA)-specific IgE titers and tissue eosinophilia, evaluation of lung function demonstrated that CD23-/- mice showed an increased AHR to methacholine (MCh) when compared to wild-ty mice but were completely resistant to the OVA challenge. Anti-CD23 Fab fragment treatment of wild-type mice did not affect the MCh-induced AHR b significantly reduced the OVA-induced airway constriction. These results im a novel role for CD23 in lung inflammation and suggest that anti-CD23 Fab fragment treatment may be of therapeutic use in allergic asthma.

PMID: 10508270 [PubMed - indexed for MEDLINE]

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2003202439. PubMed ID: 12721266. Monoclonal antibody therapy of chronic lymphocytic leukemia. Mavromatis Blanche; Cheson Bruce D. (Department of Hematology/Oncology, Lombardi Cancer Center, Georgetown University Hospital, 3800 Reservoir Rd., N.W., Washington, DC, USA. ) Journal of clinical oncology : official journal of the American Society of Clinical Oncology, (2003 May 1) 21 (9) 1874-81. Ref: 92. Journal code: 8309333. ISSN: 0732-183X. Pub. country: United States. Language: English.

AB Chemotherapeutic approaches during the last decade have failed to result in major advances in the outcome of patients with chronic lymphocytic leukemia (CLL). The recent availability of an increasing number of active monoclonal antibodies, immunotoxins, and radioimmunoconjugates (RICs) has stimulated considerable interest in clinical research in CLL. Alemtuzumab was the first antibody approved for CLL on the basis of responses in one third of patients with advanced disease. However, infusion reactions and immunosuppression with opportunistic infections present a challenge that may be overcome with altered schedules and routes of administration. Rituximab has limited activity as a single agent in patients relapsed or refractory after prior chemotherapy; however, response rates seem to be higher in previously untreated patients. More importantly, combinations with chemotherapy drugs such as fludarabine are showing promise in early trials. Newer antibodies in development as single agents and in combinations include apolizumab (Hu1D10), a humanized antibody against an epitope of HLA-DR, and IDEC-152, a primatized **anti-CD23 antibody.** BL22, an immunotoxin with impressive activity in hairy cell leukemia, is in phase II trials in CLL as well. The safe use of RICs is complicated by the elevated peripheral blood B-cell count, and the extent of bone marrow involvement in CLL; studies will explore the use of

agents to eliminate malignant cells from the bone marrow before RIC therapy. It is hoped that the rational development of combinations of the various promising antibodies with chemotherapy and each other will lead to more effective approaches for patients with CLL.

L6 ANSWER 2 OF 41 MEDLINE on STN DUPLICATE 2

2003437460. PubMed ID: 13679816. Allergic asthma and an **anti-CD23** mAb (IDEC-152): results of a phase I, single-dose, dose-escalating clinical trial. Rosenwasser Lanny J; Busse William W; Lizambri Richard G; Olejnik Teresa A; Totoritis Mark C. (University of Colorado Health Science Center and the Division of Allergy and Clinical Immunology, National Jewish Medical and Research Center, 1400 Jackson Street, Denver, CO 80206, USA. ) Journal of allergy and clinical immunology, (2003 Sep) 112 (3) 563-70. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: CD23, a cell-surface molecule, is involved in a variety of pathways likely to influence IgE production and inflammation in allergic disorders, such as allergic rhinitis and allergic asthma. OBJECTIVE: This study investigated the safety, clinical activity, and pharmacokinetic profile of IDEC-152, an IgG1 **anti-CD23 antibody**, in patients with mild-to-moderate persistent allergic asthma. METHODS: This single-dose, dose-escalating, placebo-controlled study involved 30 patients. Cohorts of 3 to 6 patients received single intravenous infusions of either placebo or IDEC-152 (0.05, 0.25, 1.0, 4.0, 10.0, or 15.0 mg/kg) on study day 1. Safety, clinical activity, and pharmacokinetics were assessed for 12 weeks after treatment. RESULTS: IDEC-152 was well tolerated. Adverse events (AEs) were mild, no grade 4 or serious AEs were reported, and no relationships were apparent between the dose of IDEC-152 and the frequency, severity, or type of event. The most common AEs in the IDEC-152 group included ecchymosis at the injection site, sinusitis, headache, arthralgia, cold syndrome, infection, throat irritation, and dysmenorrhea. Commonly reported AEs in the placebo group included headache, abdominal pain, and infection. Sustained and dose-dependent decreases in mean IgE concentrations were noted. The mean maximum concentration and area under the curve of IDEC-152 were proportional to the dose administered for the dose range 4.0 to 15.0 mg/kg. The serum half-life of the IDEC-152 antibody increased from 2 to 10 days with increasing doses. After single-dose administration of IDEC-152, no dose-dependent change in FEV(1) was observed, and most changes in peak expiratory flow rate were within 10% of baseline values. CONCLUSION: These data suggest that IDEC-152 is safe and has the potential for clinical activity in allergic asthma.

L6 ANSWER 3 OF 41 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2004:150247 Document No.: PREV200400146917. Lumiliximab (IDEC-152), an **anti-CD23 antibody**, induces apoptosis in vitro and in vivo in CLL cells. Pathan, Nuzhat [Reprint Author]; Zou, Aihua [Reprint Author]; Wynne, Dee [Reprint Author]; Chu, Peter [Reprint Author]; Thall, Aron [Reprint Author]; Byrd, John; Hanna, Nabil [Reprint Author]; Leigh, Bryan [Reprint Author]. IDEC Pharmaceuticals, San Diego, CA, USA. Blood, (November 16 2003) Vol. 102, No. 11, pp. 438a. print. Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology. CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB Lumiliximab is a macaque/human chimeric antibody that specifically recognizes CD23, the low affinity receptor for IgE on B cells. CD23 is highly upregulated in CLL cells. We have previously established that lumiliximab induces apoptosis in CD23+ B lymphoma cells and in CLL cells (Pathan, et. al., ASH 2001, 2002). Cells from 16 different CLL patients with various levels of disease and treatment histories were tested for lumiliximab-induced activation of caspase-3. Lumiliximab induced apoptosis in 14/16 CLL patient samples. Lumiliximab-induced apoptosis was associated with cleavage of caspase-3, -9 and PARP, activation of JNK and p38 kinases and downmodulation of anti-apoptotic proteins Mcl-1 and XIAP.

Lumiliximab is being tested in a dose-escalating Phase I multicenter clinical trial in CLL patients. Samples were obtained from treated patients and analyzed for in vivo induction of apoptosis in real-time. Patient samples were obtained prior to infusion of lumiliximab and 30 minutes and 2 hours following infusion on Day 1 and Day 2 of treatment. Caspase-3 activation was consistently observed 24 hours after the first infusion and prior to administration of the second infusion. No differences in caspase-3 activation were apparent within two hours after infusion of lumiliximab on Day 1 or Day 2. These data suggest that apoptosis might be a relevant in vivo mechanism of action for lumiliximab in CLL. Lumiliximab also induced decreased expression of Mcl-1 and activation of JNK and p38 kinases on Day 2 following treatment. Additional in vivo pharmacodynamic studies are underway to determine whether lumiximab-induced apoptosis in vivo occurs through similar signaling pathways as that observed in vitro.

L6 ANSWER 4 OF 41 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2004:186807 The Genuine Article (R) Number: 742UP. Lumiliximab (IDEC-152), an **anti-CD23 antibody**, induces apoptosis in vitro and in vivo in CLL cells.. Pathan N (Reprint); Zou A; Wynne D; Chu P; Thall A; Byrd J; Hanna N; Leigh B. Ohio State Univ, Columbus, OH 43210 USA; IDEC Pharmaceut, San Diego, CA USA. BLOOD (16 NOV 2003) Vol. 102, No. 11, Part 1, pp. 438A-438A. MA 1596. Publisher: AMER SOC HEMATOLOGY. 1900 M STREET. NW SUITE 200, WASHINGTON, DC 20036 USA. ISSN: 0006-4971. Pub. country: USA. Language: English.

L6 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

2004:525314 Document No. 141:52665 Lymphoid neogenesis in rheumatoid synovitis. Takemura, Seisuke (Dep. Orthop., Kansai Med. Univ., Japan). Kansai Ika Daigaku Zasshi, 55(2,3,4), 175-180 (Japanese) 2003. CODEN: KIDZAK. ISSN: 0022-8400. Publisher: Kansai Ika Daigaku Igakkai.

AB Rheumatoid synovitis was classified histochem. as diffuse synovitis (36 subjects), aggregate synovitis (13 subjects), and follicular synovitis (15 subjects) in 64 patients tested. **Anti-CD23 antibodies** and CR-2/CD21L isoform (CD21L) were pos. in follicular synovitis but neg. in diffuse synovitis and aggregate synovitis. Lymphotoxin (LT)-α, LT-β, B lymphocyte chemoattractant (BLC)/CXCL13, and secondary lymphoid chemoattractant (SLC)/CCL21 levels were significantly higher in follicular synovitis than in diffuse synovitis and aggregate synovitis. LT-βR, dendritic cell-derived C-C chemokine 1 (DC-CK1), and macrophage chemoattractant protein-1 (MCP-1) levels did not show differences among three groups of synovitis. Parameter analyses indicated that LT-β and BLC played an important role in rheumatoid synovitis. LT-β was mostly produced in B cells whereas BLC was produced in synovium cells and intravascular cells.

L6 ANSWER 6 OF 41 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2003:579125 Document No.: PREV200300580759. B lymphocyte prevalence in HIV and non-HIV infected brains. Anthony, I. C. [Reprint Author]; Crawford, D. H.; Bell, J. E. [Reprint Author]. School of Molecular and Clinical Medicine, University of Edinburgh, Edinburgh, UK. Journal of Neurovirology, (2003) Vol. 9, No. Supplement 3, pp. 90. print.
Meeting Info.: 5th International Symposium on Neuro Virology HIV Molecular and Clinical Neuroscience Workshop. Baltimore, MD, USA. September 02-06, 2003.
ISSN: 1355-0284. Language: English.

L6 ANSWER 7 OF 41 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 3

2004:181248 Document No.: PREV200400181124. Interim results from a phase I study of lumiliximab (IDEC-152, **anti-CD23 antibody**) therapy for relapsed or refractory CLL. Byrd, John C. [Reprint Author]; O'Brien, Susan; Flinn, Ian; Kipps, Thomas J.; Weiss,

Mark A.; Reid, Jennifer; Wynne, Dee; Leigh, Bryan R.. Ohio State University, Columbus, OH, USA. Blood, (November 16 2003) Vol. 102, No. 11, pp. 74a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB CD23, the low affinity IgE receptor, is constitutively expressed on the surface of CLL cells. Lumiliximab is an **anti-CD23** monoclonal antibody developed as a macaque-human chimera to minimize immunogenicity. Antitumor activity of lumiliximab was demonstrated in preclinical studies and a clinical study in CLL was initiated. Preliminary data are available from the ongoing, Phase I, dose-escalating, multicenter study assessing the safety, pharmacokinetics, and efficacy of single-agent lumiliximab therapy for relapsed or refractory CLL. Subjects are sequentially assigned to 1 of 6 treatment groups. Therapy consists of IV infusions of lumiliximab over 4 weeks as follows: 125, 250, 375, and 500 mg/m2 once weekly for treatment groups 1,2,3, and 4, respectively; 500 mg/m2 three times per week for Week 1 and 500 mg/m2 once weekly for Weeks 2-4 for treatment group 5; and 500 mg/m2 three times per week for Weeks 1-4 for treatment group 6. Data are available for the first 4 treatment groups (25 subjects). Subjects were predominantly Caucasian (88%) and male (72%), median age 60 years (47 to 79 years), and WHO Performance Status 1 (88%) at study entry. All had progressive CLL after a median of 3 prior treatment regimens (1 to 12 prior treatment regimens); 52% were fludarabine-refractory and 52% were Rai stage III/IV. Antibody infusions were administered in an outpatient setting and were well tolerated. A total of 69 study-related adverse events (probable, possible, or unknown relationship to study treatment) were reported in 16 of 25 (64%) subjects. The most common study-related adverse events were fatigue, nausea, headache, cough, and increased sweating. Two of 10 subjects in treatment group 4 had dose-limiting toxicities: Grade 4 neutropenia possibly related to treatment and Grade 4 headache probably related to treatment. Absolute lymphocyte count (ALC) reductions were observed in all treatment groups (24 of 25 subjects), with a gtoreq50% ALC decrease in 8 of 19 (42%) subjects enrolled in treatment groups 3 and 4. Reductions in lymphadenopathy were also observed. These results suggest that lumiliximab can be administered safely and may have clinical activity in subjects with heavily pretreated CLL. Accrual and response evaluations are ongoing.

L6 ANSWER 8 OF 41 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2003:553359 The Genuine Article (R) Number: 693VH. In vitro activity of lumiliximab (IDEC-152), an **anti-CD23 antibody** , in chronic lymphocytic leukemia. ANON. CLINICAL LYMPHOMA (JUN 2003) Vol. 4, No. 1, pp. 13-14. Publisher: CANCER INFORMATION GROUP, LP. 3535 WORTH ST, SAMMONS TOWER, STE 4802, DALLAS, TX 75246 USA. ISSN: 1526-9655. Language: English.

L6 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

2002:833304 Document No. 137:309495 Use of CD23 antagonists for the treatment of neoplastic disorders. Hariharan, Kandasamy; Hanna, Nabil; Braslawsky, Gary; Pathan, Nuzhat (USA). U.S. Pat. Appl. Publ. US 2002159996 A1 20021031, 42 pp., Cont.-in-part of U.S. Ser. No. 772,938. (English). CODEN: USXXCO. APPLICATION: US 2001-985646 20011105. PRIORITY: US 2001-772938 20010131.

AB Methods and kits for the treatment of neoplastic disorders comprising the use of a CD23 antagonist are provided. The CD23 antagonist may be used alone or in combination with chemotherapeutic agents. In particularly preferred embodiments the CD23 antagonists may be used to treat B cell chronic lymphocytic leukemia (B-CLL). The CD23 antagonists are **anti-CD23 antibodies**, particularly IDEC 152. IDEC 152 synergizes with chemotherapeutic agents in inducing apoptosis of cancer cells.

L6 ANSWER 10 OF 41 MEDLINE on STN DUPLICATE 4
2002224456. PubMed ID: 11962725. **Anti-CD23** monoclonal antibody inhibits germline Cepsilon transcription in B cells. Yabuuchi Shingo; Nakamura Takehiko; Kloetzer William S; Reff Mitchell E. (Seikagaku Corporation, Central Research Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) . International immunopharmacology, (2002 Mar) 2 (4) 453-61. Journal code: 100965259. ISSN: 1567-5769. Pub. country: Netherlands. Language: English.

AB A chimeric macaque/human (PRIMATIZED) **anti-CD23 antibody**, p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40 antibody-stimulated IgE production by human peripheral blood mononuclear cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE through the inhibition of germline Cepsilon RNA synthesis. Early addition of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE inhibition. In contrast, later addition of p6G5G1 still showed inhibition of increased levels of surface CD23, which is normally upregulated by stimulation with IL-4 and anti-CD40.

L6 ANSWER 11 OF 41 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2002:223261 Document No.: PREV200200223261. Inhibition of B-cell activation by delta(9)-tetrahydrocannabinol. Wallace, D. J. [Reprint author]; Quashne, R. [Reprint author]; Ryan, J. J.; Fischer-Stenger, K. J. [Reprint author]. University of Richmond, Richmond, VA, USA. Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 353. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society of Microbiology.
ISSN: 1060-2011. Language: English.

AB Delta9-tetrahydrocannabinol (THC) is known as the major psychoactive component of marijuana and it is now clear that cannabinoids and cannabinoid-related molecules are also involved in immune regulation. By binding to cannabinoid-specific receptors, these molecules have been shown to decrease the proliferation of lymphocytes and reduce antibody production by B-lymphocytes. However, the mechanisms responsible for these effects are not clearly understood. Interleukin-4 (IL-4) is a pleiotropic cytokine produced by TH2-cells that is known to induce the proliferation of B-lymphocytes and induce antibody production by these cells. IL-4 has also been shown to increase the expression of CD23 (low affinity IgE receptor) on the surface of B-cells. Therefore, the expression of CD23 can be used as a marker for B-cell activation. The purpose of this study was to determine whether THC inhibits B-cell activation induced by IL-4 stimulation. The M-12 murine B-cell line and the WIL-2 human B-cell line were plated in 96-well microtiter plates (4X104 cells/well) and incubated in the presence of THC (0.01-10 muM) and simultaneously stimulated with IL-4 (0.5-5 ng/ml) for 24 to 48 hours. The cells were then stained with FITC-labeled **anti-CD23 antibody** and analyzed by flow cytometry to detect the expression of CD23 on the surface of the B-cells. These studies demonstrated that triggering with 5 ng/ml of IL-4 for 48 hours induced peak levels of CD23 expression on the B-cells. Exposure to THC downregulated the expression of CD23 on murine B-cells (mean fluorescence intensity: 34 with IL-4 alone, 14 with IL-4 and THC) and to a lesser degree on human B-cells (mean fluorescence intensity: 65 with IL-4 alone, 48 with IL-4 and THC). These results suggest that THC inhibits B-cell activation induced by IL-4 stimulation which may be responsible for the drug-induced decrease in antibody production observed in B-lymphocytes.

L6 ANSWER 12 OF 41 MEDLINE on STN DUPLICATE 5
2001403419. PubMed ID: 11454061. Endocytosis and recycling of the complex

between CD23 and HLA-DR in human B cells. Karagiannis S N; Warrack J K; Jennings K H; Murdock P R; Christie G; Moulder K; Sutton B J; Gould H J. (The Randall Centre for Molecular Mechanisms of Cell Function, King's College London, UK.. hjg@helios.rai.kcl.ac.uk) . Immunology, (2001 Jul) 103 (3) 319-31. Journal code: 0374672. ISSN: 0019-2805. Pub. country: England: United Kingdom. Language: English.

AB The presentation of extremely low doses of antigen to T cells is enhanced by immunoglobulin E (IgE)-dependent antigen focusing to CD23, the low-affinity receptor for IgE, expressed on activated B cells. CD23 contains a C-type lectin domain in its extracellular sequence and a targeting signal for coated pits, required for endocytosis, in its cytoplasmic sequence. CD23 is non-covalently associated with the major histocompatibility complex class II antigen, human leucocyte antigen HLA-DR, on the surface of human B cells, but the fate of this complex following endocytosis is unknown. To answer this question we have labelled these proteins on the surface of RPMI 8866 B cells and traced their route through the cytoplasm. Endocytosis mediated by **anti -CD23 antibodies** (BU38 and MHM6) led to the loss of CD23 from the cells. Endocytosis mediated by an antibody to HLA-DR (CR3/43) or an antigen-IgE complex (NP-BSA-anti-NP IgE), however, led to recycling of the HLA-DR-CD23 complex to the cell surface on a time scale (3-6 hr) consistent with the recycling of HLA-DR in antigen presentation. Along the latter pathway CD23 label was observed in cytoplasmic organelles that resembled the 'compartments for peptide loading' or 'class II vesicles' described by previous authors. Two features of the recycling process may contribute to the efficiency of antigen presentation. Peptide exchange may be facilitated by the proximity of HLA-DR and antigen in peptide loading compartments of the endosomal network. The return of CD23 with HLA-DR to the cell surface may then help to stabilize specific B-cell-T-cell interactions, contributing to T-cell activation.

L6 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

2000:457197 Document No. 133:57697 Enhanced proteins production in cell culture stimulated by unusually low alkanoic acid concentrations. Islam, Seema; Sharp, Nigel Alan (Glaxo Group Limited, UK). PCT Int. Appl. WO 2000039282 A1 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP10157 19991221. PRIORITY: GB 1998-28624 19981223.

AB A process is provided for the production of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium containing an alkanoic acid or its salt at a maintained concentration of less than 0.1mM. Thus, NSO cells transfected with an IgG1 humanized **anti-CD23 antibody** was cultured for 56 days in a draw and fill repeated batch mode in a medium containing 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in antibody production over the control.

L6 ANSWER 14 OF 41 MEDLINE on STN DUPLICATE 6

2001015588. PubMed ID: 11018076. Enhanced intestinal transepithelial antigen transport in allergic rats is mediated by IgE and CD23 (FcepsilonRII). Yang P C; Berin M C; Yu L C; Conrad D H; Perdue M H. (Intestinal Disease Research Program and Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada. ) Journal of clinical investigation, (2000 Oct) 106 (7) 879-86. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB We previously reported that active sensitization of rats resulted in the appearance of a unique system for rapid and specific antigen uptake across intestinal epithelial cells. The current studies used rats sensitized to

horseradish peroxidase (HRP) to define the essential components of this antigen transport system. Sensitization of rats to HRP stimulated increased HRP uptake into enterocytes (significantly larger area of HRP-containing endosomes) and more rapid transcellular transport compared with rats sensitized to an irrelevant protein or naive control rats. Whole serum but not IgE-depleted serum from sensitized rats was able to transfer the enhanced antigen transport phenomenon. Immunohistochemistry demonstrated that sensitization induced expression of CD23, the low-affinity IgE receptor (FcepsilonRII), on epithelial cells. The number of immunogold-labeled CD23 receptors on the enterocyte microvillous membrane was significantly increased in sensitized rats and was subsequently reduced after antigen challenge when CD23 and HRP were localized within the same endosomes. Finally, pretreatment of tissues with luminally added **anti-CD23 antibody** significantly inhibited both antigen transport and the hypersensitivity reaction. Our results provide evidence that IgE antibodies bound to low-affinity receptors on epithelial cells are responsible for the specific and rapid nature of this novel antigen transport system.

L6 ANSWER 15 OF 41 MEDLINE on STN DUPLICATE 7
2000150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by **anti-CD23** monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan. ) International journal of immunopharmacology, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) monoclonal antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact **anti-CD23 antibody** in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which **anti-CD23 antibodies** inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

L6 ANSWER 16 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
1999:736930 Document No. 131:350265 Antibodies to CD23. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the preparation and characterization of murine monoclonal and humanized antibodies which bind to the CD23 (FcεRII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to CD23 with association rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these antibodies may find use in the treatment of autoimmune and inflammatory disorders.

L6 ANSWER 17 OF 41 MEDLINE on STN DUPLICATE 8
1999319375. PubMed ID: 10390902. Degranulation of eosinophils by IgG antibody to Candida antigen. Ikeda Y; Mita H; Kudo M; Hasegawa M; Akiyama K. (Department of Clinical Research, National Sagamihara Hospital. ) Arerugi = [Allergy], (1999 May) 48 (5) 546-53. Journal code: 0241212. ISSN: 0021-4884. Pub. country: Japan. Language: Japanese.

AB The pathophysiological role of IgG antibody to fungi antigen widely distributed in environment such as Candida albicans in bronchial asthma has not been clarified. Wells of microtiter plate were coated with the extract of Candida albicans and then IgG antibody was immobilized on the wells by incubation with patient's serum. After cultivation of eosinophils on the well, degranulation of eosinophils, as assessed by quantitation of EPX in the supernatant, has been observed. Degranulation was completely abrogated after depletion of IgG in the serum and also decreased by incubation of the cells with anti-CD32 antibody, or anti-CD18 antibody, but not **anti-CD23 antibody.**
Immune complex, which had been prepared by incubation of the extract of Candida albicans with patient's serum, also evoked degranulation of eosinophils. We have examined whether degranulation can be induced by two purified antigens of Candida albicans, i.e., mannan A and acid protease. IgG antibody to acid protease was detected at no or minimal levels in most sera and the antigen did not induce degranulation. On the other hand, mannan A induced degranulation. This observation may be due to response for the presence of IgG antibody to mannan A in the sera. These results suggest that immobilized IgG induced degranulation of eosinophils through Fc gamma RII (CD 32) on eosinophils and mannan A is a major allergen associated with IgG-induced eosinophil degranulation.

L6 ANSWER 18 OF 41 MEDLINE on STN DUPLICATE 9
1999135997. PubMed ID: 9949321. Production of chemokines and proinflammatory and antiinflammatory cytokines by human alveolar macrophages activated by IgE receptors. Gosset P; Tillie-Leblond I; Oudin S; Parmentier O; Wallaert B; Joseph M; Tonnel A B. (Unite INSERM U416, Institut Pasteur, Lille, France. ) Journal of allergy and clinical immunology, (1999 Feb) 103 (2 Pt 1) 289-97. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: The alveolar macrophage (AM) expresses the low affinity IgE receptor and has the ability to produce not only several proinflammatory cytokines (TNF-alpha, IL-1, IL-6) but also antiinflammatory cytokines (IL-1 receptor antagonist [IL-1ra], IL-10), chemokines (IL-8, monocyte chemotactic protein-1 [MCP-1]), and macrophage inflammatory protein-1alpha (MIP-1alpha). OBJECTIVE: The aim of this study was to evaluate the capacity of the AM from patients with allergic asthma and control subjects to produce chemokines and antiinflammatory versus proinflammatory cytokines after activation by IgE receptors and to define the role of CD23 in this activation. METHODS: AMs were collected by bronchoalveolar lavage from 13 patients with allergic asthma and 14 healthy subjects. Adherent AMs were activated either by the successive addition of IgE and anti-IgE or by monoclonal mouse IgG **anti-CD23** or by a control monoclonal mouse antibody. TNF, IL-1beta, IL-1ra, IL-10, IL-8, MCP-1, and MIP-1alpha levels were evaluated in supernatants of AMs incubated for 18 hours and in some cases after 4 hours of incubation. RESULTS: Activation by IgE and anti-IgE antibodies significantly increased the production of TNF, IL-1beta, IL-8, MCP-1, MIP-1alpha, and IL-10 in both control subjects and patients with asthma, whereas the increase for IL-1ra was only significant for the control subjects. Whereas F(ab) fragments of **anti-CD23 antibodies** inhibited IgE plus

anti-IgE-induced cytokine production, activation by monoclonal IgG **anti-CD23 antibodies** reproduced the effect of IgE immune complexes. At 4 hours, the secretion of proinflammatory cytokines was increased by activation by IgE receptors, in contrast to antiinflammatory cytokines. In addition, analysis of the balance between proinflammatory and antiinflammatory cytokines showed that IgE-dependent activation largely favored the proinflammatory cytokines, particularly in patients with asthma. CONCLUSION: IgE-dependent activation by the FcepsilonRII receptor upregulates the synthesis of both chemokines and antiinflammatory cytokines in addition to proinflammatory cytokines. However, AMs from patients with allergic asthma may promote airway inflammation after activation by IgE receptors through its preferential effect on proinflammatory cytokines.

L6 ANSWER 19 OF 41 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

1999:1848 Document No.: PREV199900001848. Binding of **anti-CD23** monoclonal antibody to the leucine zipper motif of FcepsilonRII/CD23 on B cell membrane promotes its proteolytic cleavage. Evidence for an effect on the oligomer/monomer equilibrium. Munoz, Olivier; Brignone, Chrystelle; Grenier-Brossette, Nicole; Bonnefoy, Jean-Yves; Cousin, Jean-Louis [Reprint author]. INSERM U343, Hopital de l'Archet, B.P. 79, F-06202 Nice cedex 03, France. Journal of Biological Chemistry, (Nov. 27, 1998) Vol. 273, No. 48, pp. 31795-31800. print. CODEN: JBCHA3. ISSN: 0021-9258. Language: English.

AB In the present study we have compared the binding of two monoclonal antibodies to CD23, EBVCS1 and mAb25, which recognize the stalk and the lectin domain, respectively, on the CD23 molecule. At 4degreeC, EBVCS1 binds to about 10% of the receptors recognized by mAb25 on the B cell surface. At 37degreeC, whereas mAb25 reaches its maximal binding within a few seconds, EBVCS1 requires 60 min to bind to the same extent. Stabilization of the oligomeric structure of CD23 with IgE strongly affects in a dose-dependent fashion the number of binding sites seen by EBVCS1 but not the t1/2 to reach them, suggesting that EBVCS1 binds to the coiled coil region through an allosteric mechanism. EBVCS1 rapidly down-modulates the membrane CD23 expression with a coincident increase of CD23-soluble fragments in the culture medium, an effect that is inhibited by IgE. In contrast, mAb25, as well as IgE, protects CD23 from proteolytic cleavage and stimulates its endocytosis. These results suggest that EBVCS1 unravels the coiled coil structure of CD23, rendering it more susceptible to proteolytic attack. This supports the oligomeric model proposed previously (Gould, H., Sutton, B., Edmeades, R., and Beavil, A. (1991) Monogr. Allergy 29, 28-49). The biological significance of these observations is discussed.

L6 ANSWER 20 OF 41 MEDLINE on STN DUPLICATE 10

97370982. PubMed ID: 9227207. Increased number of IgE positive Langerhans cells in the conjunctiva of patients with atopic dermatitis. Yoshida A; Imayama S; Sugai S; Kawano Y; Ishibashi T. (Department of Ophthalmology, Faculty of Medicine, Kyushu University, Fukuoka, Japan. ) British journal of ophthalmology, (1997 May) 81 (5) 402-6. Journal code: 0421041. ISSN: 0007-1161. Pub. country: ENGLAND: United Kingdom. Language: English.

AB AIM: To determine the role of Langerhans cells (LCs) found to bear IgE in patients with atopic dermatitis (AD) by evaluating the surface distribution of these cells in the conjunctival epithelium and epidermis of skin lesions in patients with AD. METHODS: The double labelling method was used to evaluate IgE positive cells that were positive for anti-CD1a or **anti-CD23 antibody** in an epithelial sheet of the conjunctival limbus. Specimens of conjunctiva were obtained from 12 men, six of whom had AD and ocular complications. Five patients without atopic disease served as controls, plus one additional patient with asthma but no AD. A similar study was conducted using epidermal sheets obtained from two patients with AD and from one without AD. RESULTS: The number of CD1a+ cells present in the conjunctival epithelium of the patients with AD significantly exceeded that of the patients

without AD. Most CD1a+ cells in the conjunctival epithelium and epidermis from the patients with AD bore IgE on their surfaces. Few such cells from patients without AD bore IgE. No CD23+ cells were found in the patients with or without AD. CONCLUSIONS: The presence of an increased number of LCs bearing IgE on their surfaces in the conjunctival epithelium of patients with AD suggests that these cells may be involved in eliciting the hypersensitivity reaction and participate in ocular inflammation.

L6 ANSWER 21 OF 41 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 11

1997:415432 Document No.: PREV199799707475. Involvement of both protein kinase C and G proteins in superoxide production after IgE triggering in guinea pig eosinophils. Aizawa, Toshiya [Reprint author]; Tamura, Gen; Sanpei, Ken-Ichi; Shibasaki, Atsushi; Shirato, Kunio; Takishima, Tamotsu. Fukushima Cent. Hosp., Yoshikura Aza Yachi 52, Fukushima City 960, Japan. Allergology International, (1997) Vol. 46, No. 2, pp. 91-99. ISSN: 1323-8930. Language: English.

AB To study the function and mechanism of eosinophils via the low affinity IgE receptor (FC-epsilon-RII), we examined the production of O-2 metabolites by measuring the luminol-dependent chemiluminescence (LDCL) response and the generation of cysteinyl leukotrienes. Eosinophils obtained from guinea pig peritoneal fluid sensitized with horse serum were purified. Luminol-dependent chemiluminescence was induced by stimulation with monoclonal **anti-CD23 antibody**, but not by mouse serum (controls). The mean (+-SEM) value of LDCL was 20.6+-1.3 times 10-3c.p.m. This reaction consisted of an initial rapid phase and a propagation phase and ended within 10min. Guinea pig eosinophils were histochemically stained with monoclonal **anti-CD23 antibody.** The major product generated in the LDCL response was superoxide, as determined by the measurement of superoxide by cytochrome c reduction and the complete inhibitory effect of superoxide dismutase on the LDCL response. Pretreatment with either pertussis toxin or cholera toxin inhibited the LDCL reaction. Depletion of bivalent ions by EDTA inhibited this response and the protein kinase C inhibitor D-Sphingosin inhibited both 1-oleoyl-2acetyl-glycerol-induced and FC-epsilon-RII-mediated LDCL. These findings suggest that the NADPH-protein kinase C pathway may be involved in the Fc-epsilon-RII-mediated LDCL response in guinea pig eosinophils.

L6 ANSWER 22 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN

1996:380155 Document No. 125:31943 Binding agents to CD23. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD23 useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized antibody or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal **anti-CD23 antibody**, CD23-liposomes bind to CD14+ mononuclear cells and α chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal antibodies decrease CD23-liposome binding to activated blood monocytes, increases of monocyte nitrate production, oxidative burst and cytokine production by binding recombinant CD23 to CD11b and CD11c, etc.

L6 ANSWER 23 OF 41 MEDLINE on STN DUPLICATE 12

96409286. PubMed ID: 8814268. Regulation of B cell growth and differentiation via CD21 and CD40. Axcrona K; Gray D; Leanderson T.

(Department of Cell and Molecular Biology, Lund University, Sweden.. Karol.Axcrona@immuno.lu.se) . European journal of immunology, (1996 Sep) 26 (9) 2203-7. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Stimulation in vitro of murine splenic B cells by lipopolysaccharide, anti-kappa Sepharose, anti-CD40 or allo-reactive T helper cells all up-regulated CD21 and CD23 surface expression. Neither anti-CD21 nor **anti-CD23 antibodies** induced B cell growth or differentiation when added in soluble form or coupled to Sepharose. However, anti-CD40-stimulated B cells showed increased proliferation in the presence of anti-CD21 antibodies coupled to Sepharose; co-stimulation via CD21 also induced differentiation to immunoglobulin secretion in a fraction of anti-CD40-stimulated B cells. Furthermore, anti-CD40 antibodies inhibited differentiation to immunoglobulin secretion induced by lipopolysaccharide and, hence, appears to be a dominant negative signal for B cell differentiation.

L6 ANSWER 24 OF 41 MEDLINE on STN DUPLICATE 13

97137431. PubMed ID: 8982768. Differential regulation of antigen-specific IgG4 and IgE antibodies in response to recombinant filarial proteins. Garraud O; Nkenfou C; Bradley J E; Nutman T B. (Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, MD 20892, USA. ) International immunology, (1996 Dec) 8 (12) 1841-8. Journal code: 8916182. ISSN: 0953-8178. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Having identified two recombinant filarial proteins (Ov27 and OvD5B) that induced patient peripheral blood mononuclear cells to produce antigen-specific IgG4/IgE antibodies in vitro, we assessed the role these filarial antigens play in inducing antigen-specific isotype switching (gamma 4 and epsilon) in the absence of T cells. Purified CD19+ s gamma-/s epsilon- B cells were cultured with either of these antigens in the presence of anti-CD40 mAb and human IL-4. Both antigen and polyclonal signals delivered by IL-4 (or IL-13) were necessary for the induction of specific IgG4/IgE antibodies. To assess the role played by cytokines produced by B lymphocytes in antigen-driven selection of the gamma 4 or epsilon isotype, neutralizing anti-cytokine antibodies were used in vitro. While anti-IL-12 antibodies did not alter the antigen-specific IgG4/IgE production, anti-IL-6, anti-IL-13 and anti-tumor necrosis factor-alpha antibodies significantly inhibited the production of IgG4/IgE. Anti-IL-2 and anti-IL-10 antibodies appeared to down-regulate antigen-specific IgG4 antibodies without affecting antigen-specific IgE antibodies. Although anti-CD21 antibodies had no effect on specific IgE antibodies, they up-regulated specific IgG4 antibodies, a finding paralleled by **anti-CD23 antibodies.** These data suggest that certain filarial antigen-specific IgG4/IgE responses can be differentially regulated and that certain endogenously produced molecules from B cells-such as IL-2, IL-10, CD23 and CD21-play a significant role in the induction of specific isotypes of antigen-specific antibodies.

L6 ANSWER 25 OF 41 MEDLINE on STN DUPLICATE 14

96071560. PubMed ID: 7585180. Marked amelioration of established collagen-induced arthritis by treatment with antibodies to CD23 in vivo. Plater-Zyberk C; Bonnefoy J Y. (Glaxo Institute for Molecular Biology, Immunology Department, Geneva, Switzerland. ) Nature medicine, (1995 Aug) 1 (8) 781-5. Journal code: 9502015. ISSN: 1078-8956. Pub. country: United States. Language: English.

AB CD23 is a low-affinity receptor for immunoglobulin E (IgE) expressed by a variety of haematopoietic cells. Proteolytic cleavage of the transmembrane receptor generates soluble forms, which can be detected in biological fluids. CD23 regulates many functional aspects of immune cells, both in its cell-associated and soluble forms. In view of the increased levels of CD23 in rheumatoid arthritis, we have studied the effect of neutralizing CD23 in type II collagen-induced arthritis in mice, a model for human rheumatoid arthritis. Successful disease modulation is achieved by treatment of arthritic DBA/1 mice with either polyclonal or

monoclonal antibodies to mouse CD23. Treated mice show a dose-related amelioration of arthritis with significantly reduced clinical scores and number of affected paws. This improvement in clinical severity is confirmed by histological examination of the arthritic paws. A marked decrease in cellular infiltration of the synovial sublining layer and limited destruction of cartilage and bone is evident in animals treated with therapeutic doses of **anti-CD23 antibody** . These findings demonstrate the involvement of CD23 in a mouse model of human rheumatoid arthritis.

L6 ANSWER 26 OF 41 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

1995:521449 Document No.: PREV199598535749. Treatment with antibodies to CD23 markedly ameliorates an established collagen-induced arthritis in mice. Plater-Zyberk, Christine; Bonnefoy, Jean-Yves. Glaxo IMB, Immunol. Dep., 14 Chemin Des Aulx, CH-1228 Geneva, Switzerland. Arthritis and Rheumatism, (1995) Vol. 38, No. 9 SUPPL., pp. S310.
Meeting Info.: 59th National Scientific Meeting of the American College of Rheumatology and the 30th National Scientific Meeting of the Association of Rheumatology Health Professionals. San Francisco, California, USA. October 21-26, 1995.
CODEN: ARHEAW. ISSN: 0004-3591. Language: English.

L6 ANSWER 27 OF 41 MEDLINE on STN DUPLICATE 15

95317800. PubMed ID: 7797246. Functional significance of CD23- on CD23-transfected Th2 clone. Nambu M; Hagen M; Sandor M; Sacco R E; Kwack K; Lynch R G. (Department of Pathology, College of Medicine, University of Iowa, Iowa City 52242, USA. ) Immunology letters, (1995 Jan) 44 (2-3) 163-7. Journal code: 7910006. ISSN: 0165-2478. Pub. country: Netherlands. Language: English.

AB CD23, a low-affinity IgE Fc receptor, is not displayed on most resting T cells but its expression has been shown to be transiently induced in vivo and in vitro on some CD4+ T cells [1-4] and in vivo on CD8+ T cells by IgE-secreting hybridoma tumors [5]. To investigate the functional role of CD23 on T cells, we inserted a CD23 construct into an expression vector driven by a CD2 promoter and transfected it into a murine Th2 clone D10.G4.1 (D10). We stimulated the transfected D10 cells (D10.3M.24) with anti-TCR antibody in the presence or absence of IgE, and measured IL-4, IL-5 and IL-6 production in the culture supernatants. Activation of D10.3M.24 cells by anti-TCR antibody induced greater levels of IL-4, IL-5 and IL-6 production, when the TCR and CD23 were co-crosslinked by TNP anti-TCR and IgE anti-TNP antibodies. IgG anti-TNP antibody did not enhance lymphokine production by D10.3M.24 cells. The enhanced lymphokine production by IgE was blocked by monoclonal **anti-CD23 antibody.** IgE anti-TNP antibody did not enhance lymphokine production by the wild-type D10 cells induced by TNP anti-TCR antibody. These studies show that when co-crosslinked with the TCR, CD23 can modulate the lymphokine production in activated Th2 cells. Since CD23 binds to IgE and also binds to CD21 [6], a complement receptor commonly expressed on B cells, T-cell CD23 could play an immunoregulatory role during cognate T-B cell interaction and during IgE antibody responses.

L6 ANSWER 28 OF 41 MEDLINE on STN DUPLICATE 16

96159495. PubMed ID: 8589271. Involvement of CD23/Fc epsilon RII in the homotypic and heterotypic cytoadhesion of the human eosinophilic cell line Eol-3. Yamaoka K A; Kolb J P. (U 365 INSERM, Interferons et Cytokines, Institut Curie, Paris, France. ) European cytokine network, (1995 May-Jun) 6 (3) 145-55. Journal code: 9100879. ISSN: 1148-5493. Pub. country: France. Language: English.

AB A subclone of the EoL-3 human eosinophilic leukemia cell line (EoL-3.12) was selected for its high inducibility of CD23 (low affinity IgE receptor/Fc epsilon RII) by IL-4. Maximum membrane CD23 expression was detected after 16 h of incubation with IL-4, then gradually returned to basal level after 48 h. Membrane expression of CD23 on EoL-3.12 cells was found to parallel their homotypic aggregation. Extending the time of

incubation with IL-4 to 48 h or more resulted in a de-aggregation of cells of cells with a shedding of membrane CD23 and an increase of its soluble form, sCD23. The IL-4-induced aggregation of EoL-3.12 cells was inhibited with **anti-CD23 antibody** or human myeloma IgE protein, indicating that it was mediated through the engagement of CD23. EoL3.12 incubated with IL-4 displayed morphological changes associated with differentiation, such as an increased number of lobulated nuclei with prominent nucleoli, increased ratio of cytoplasm and distinct cytoplasmic processes. EoL-3.12 cells incubated with IL-4 also displayed an enhanced adherence to human umbilical vein endothelial cells (HUVEC), which was reverted when the IL-4 incubation time extended. Furthermore, the transendothelial migration of EoL-3.12 cells toward a chemokinetic gradient of soluble CD23 (sCD23; 29 kDa fragment) closely paralleled the density of membrane CD23 expressed on EoL-3.12 cells. Additionally, the engagement of CD23 led to the activation of the L-arginine-dependent pathway of nitric oxide (NO) production, as detected by the increase in intracytoplasmic cGMP concentration. The capacity of EoL-3.12 cells to form homotypic as well as heterotypic adhesion appears therefore to be regulated, at least in part, by the level of CD23 expression.

L6 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2004 ACS on STN
1994:296620 Document No. 120:296620 Induction of B cell and T cell tolerance in vivo by **anti-CD23** mAb. Morris, Suzanne C.; Lees, Andrew; Holmes, Joanne M.; Jeffries, Ramona D. A.; Finkelman, Fred D. (Dep. Med., Uniformed Serv. Univ. Health Sci., Bethesda, MD, 20814, USA). Journal of Immunology, 152(8), 3768-76 (English) 1994. CODEN: JOIMA3. ISSN: 0022-1767.

AB T cell tolerance can be induced by B cell presentation of Ags to naive T cells. To further characterize this mechanism of T cell tolerance induction, the authors have investigated the effects of injecting mice with an intact rat IgG2a Ab, which binds to the B cell low-affinity Fcε receptor (CD23), on the responsiveness of B cells and T cells to rat IgG2a. The authors' observations indicate that (1) i.v., s.c., or i.p. injection of this Ab induces antigen-specific B cell and T cell tolerance; (2) both forms of tolerance are induced more completely by injection of rat IgG2a **anti-CD23** mAb than by injection of an equal dose of a control rat IgG2a Ig; and (3) reduced responsiveness to Ag is seen as early as 1-3 days after **anti-CD23** mAb injection and reaches maximum levels by 7 days after injection. Although tolerance induced by the injection of soluble proteins has been reported to be characterized by reduced production of IL-2 and IFN-γ, but normal production of IL-4, injection of mice with rat IgG2a anti-mouse CD23 mAb greatly decreases the IL-4 response to a rat IgG2a immunogen that normally induces a large IL-4 response.

L6 ANSWER 30 OF 41 MEDLINE on STN DUPLICATE 17
93121641. PubMed ID: 8380367. Defective expression of CD23 and autocrine growth-stimulation in Epstein-Barr virus (EBV)-transformed B cells from patients with Wiskott-Aldrich syndrome (WAS). Simon H U; Higgins E A; Demetriou M; Datti A; Siminovitch K A; Dennis J W. (Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario, Canada. ) Clinical and experimental immunology, (1993 Jan) 91 (1) 43-9. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB WAS is an X-linked, recessive, immune deficiency syndrome, characteristically associated with lymphocyte and platelet dysfunction. Peripheral B lymphocytes from WAS patients are nonresponsive to polysaccharide antigens and show reduced numbers of cells expressing the integral membrane glycoprotein, CD23. The release of CD23 proteolytic fragments, so-called soluble CD23 (sCD23), by B lymphoblasts and EBV-transformed B cell lines has previously been described, and these fragments have been shown to stimulate autocrine growth of these cells. We have found that the surface expression of CD23 is reduced on WAS compared with control EBV-B cells. Surface CD23 levels were reduced two-fold in four WAS cell lines (group I) and nine-fold in four other

lines (group II). Group II WAS cell lines also showed reduced growth rates in serum-free medium when compared with group I cell lines and EBV-B cell lines from eight normal subjects. In contrast to the group II WAS lines, group I and EBV-B cells from normal individuals produced an autocrine-growth factor activity which could be absorbed by **anti -CD23 antibodies.** Immunoprecipitation of sCD23 from culture supernatants confirmed that group I WAS cell lines produced less sCD23, particularly the 37K fragment which was prevalent in control EBV-B cells. Northern analysis showed that CD23 mRNA levels were increased three-fold in group I and unchanged in group II WAS compared with normal EBV-B cell lines, suggesting that decreased surface expression in WAS EBV-B cells reflects post-transcriptional events. Together these results suggest that reduced cell surface expression and aberrant proteolysis of CD23 occurs in WAS patients' B lymphocytes and may contribute to impaired immune function in these patients.

L6 ANSWER 31 OF 41 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 18

1992:292840 Document No.: PREV199243005190; BR43:5190. **ANTI-CD23 ANTIBODY** INDUCES ANTIGEN-SPECIFIC T CELL TOLERANCE IN-VIVO. FINKELMAN F D [Reprint author]; LEES A; MORRIS S C. DEP MED, USUHS, BETHESDA, MD 20814, USA. FASEB Journal, (1992) Vol. 6, No. 5, pp. A1699.
Meeting Info.: MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY (FASEB) PART II, ANAHEIM, CALIFORNIA, USA, APRIL 5-9, 1992. FASEB (FED AM SOC EXP BIOL) J.
CODEN: FAJOEC. ISSN: 0892-6638. Language: ENGLISH.

L6 ANSWER 32 OF 41 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 19

1992:249215 Document No.: PREV199242119515; BR42:119515. MONOCLONAL **ANTI-CD23 ANTIBODIES** INHIBIT IL-6 RELEASE FROM ANTI-MU STIMULATED B CELLS. LING Z-D [Reprint author]; WEBB B T; YEOH E; MATHESON D S. DIV INFECT IMMUNOL DIS, DEP PAEDIATRICS, UNIV BRITISH COLUMBIA, BC'S CHILDREN'S HOSP, VANCOUVER, CAN. FASEB Journal, (1992) Vol. 6, No. 4, pp. A1079.
Meeting Info.: 1992 MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY (FASEB), PART I, ANAHEIM, CALIFORNIA, USA, APRIL 5-9, 1992. FASEB (FED AM SOC EXP BIOL) J.
CODEN: FAJOEC. ISSN: 0892-6638. Language: ENGLISH.

L6 ANSWER 33 OF 41 MEDLINE on STN DUPLICATE 20

93228867. PubMed ID: 1299237. Studies on the role of interleukin-4 and Fc epsilon RII in the pathogenesis of minimal change nephrotic syndrome. Cho B S; Lee C E; Pyun K H. (Department of Pediatrics, College of Medicine, Kyung Hee University, Seoul, Korea. ) Journal of Korean medical science, (1992 Dec) 7 (4) 343-8. Journal code: 8703518. ISSN: 1011-8934. Pub. country: KOREA. Language: English.

AB Childhood minimal change nephrotic syndrome (MCNS) has often been associated with allergic symptoms such as urticaria, bronchial asthma, atopic dermatitis, allergic rhinitis and elevated IgE levels and referred to involve immune dysfunction. Fc epsilon RII is known to be involved in IgE production and response. Interleukin-4 is being recognized as a major cytokine up-regulating IgE production. Hence the present study is aimed at investigating the role of interleukin-4 and Fc epsilon RII in the pathogenesis of MCNS. IgE was measured by ELISA. Fc epsilon RII was analyzed by fluorescence activated cell scanner (FAC-scan) by double antibody staining with anti Leu16-FITC and anti Leu20-PE. Soluble IgE receptor was measured by ELISA using **anti CD23 antibody** (3-5-14). Interleukin-4 activities were measured by CD23 expression on purified human tonsillar B cells. Serum IgE levels were significantly higher in MCNS (1,507 +/- 680 IU/dl) than in normal controls (123 +/- 99.2 IU/dl). A significantly higher expression of membrane Fc epsilon RII was noted for MCNS (41 +/- 12%) than that in normal controls (18 +/- 6.2%) ($p < 0.001$). Soluble CD23 levels were also significantly

higher in MCNS (198 +/- 39.3%) than in normal controls (153 +/- 13.4) ($p < 0.01$). Interleukin-4 activity in sera of MCNS (12U/ml) was also significantly higher than normal controls (4.5U/ml). These results indicate that increased production of Fc epsilon RII and interleukin-4 may play an important role in the pathogenesis of MCNS.

L6 ANSWER 34 OF 41 MEDLINE on STN DUPLICATE 21
91170762. PubMed ID: 1826018. Cross-linking of CD23 antigen by its natural ligand (IgE) or by **anti-CD23 antibody** prevents B lymphocyte proliferation and differentiation. Luo H Y; Hofstetter H; Banchereau J; Delespesse G. (University of Montreal, Notre-Dame Hospital, Research Center, Canada. ) Journal of immunology (Baltimore, Md. : 1950), (1991 Apr 1) 146 (7) 2122-9. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The possible role of CD23 in the activation of human B lymphocytes was systematically investigated by examining the effect of: 1) **anti-CD23** mAb; 2) IgE or IgE-immune complexes and; 3) native or recombinant soluble CD23 of different m.w., on B cell proliferation. Intact **anti-CD23** mAb or its F(ab')2 fragments inhibit the proliferation of tonsillar B lymphocytes costimulated with either Staphylococcus aureus Cowan I (SAC) or anti-IgM and IL-4. The antibody has no effect when IL-2 or LMW-BCGF is used as the second stimulant. The response of IL-4-pretreated B cells (expressing high levels of CD23) to anti-IgM together with IL-2 or B cell-derived B cell growth factor is inhibited by **anti-CD23** mAb, indicating that this antibody prevents B cell activation regardless of the B cell activators but provided that the density of CD23 on B cells is sufficient. **Anti-CD23** mAb markedly inhibits DNA synthesis only when added during the first 12 h of the culture and has no effect on the ongoing proliferation of CD23-bearing B cell blasts (SAC induced and IL-4 supported or EBV transformed). Monovalent Fab fragments of **anti-CD23** mAb are inactive unless they are used in tandem with goat anti-mouse Fab suggesting that the inhibition is due to cross-linking of surface CD23. Most interestingly, polymeric IgE or IgE-immune complexes have the same effect as **anti-CD23** and moreover they inhibit IgM production by SAC and IL4-stimulated B cells. The inhibiting effect of IgE or of **anti-CD23** mAb is not due to their neutralization of soluble CD23 because these failed to display B cell growth factor activity under various experimental conditions. It is concluded that IgE-immune complexes may regulate activation and differentiation of CD23-bearing surfaceIgM/surfaceIgD precursor B lymphocytes.

L6 ANSWER 35 OF 41 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 22
91:364397 The Genuine Article (R) Number: FT273. IGE AND SWITCHING PHENOMENA. BONNEFOY J Y (Reprint). GLAXO INST MOLEC BIOL, CHEMIN AULX, CH-1228 PLAN LES OUATES, SWITZERLAND (Reprint). SEMAINE DES HOPITAUX (1991) Vol. 67, No. 26-2, pp. 1199-1200. Pub. country: SWITZERLAND. Language: French.
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB In allergic disorders, IgE increases following allergen stimulation. In vitro IgE synthesis is the result of a complex interaction between T-cells, B-cells and monocytes, controlled by cytokines produced by T-cells and monocytes (IL-4, IL-5, IFN-gamma, and IL-6). IL-4 acts as a switching factor to induce synthesis of IgE. IFN-gamma inhibits IL-4 induced IgE synthesis. IL-4 is a mastocyte growth factor, as well as IL-3. Moreover, IL-4 is a potent inducer of FceR/CD23 expression of B-cells and monocytes. Monoclonal **anti-CD23 antibodies** inhibit IL-4-induced IgE synthesis in an isotype-specific manner. IL-4-producing T-cells also produce IL-5 which induces differentiation of eosinophil precursors. Eosinophils, in turn, express low affinity receptors for IgE when activated. Activation of the IgE system thus leads to increased IgE production and increased expression of IgE receptors. This results in increased receptor-ligand interactions, resulting in release of numerous chemical mediators involved in the

pathogenesis of allergic disorders.

L6 ANSWER 36 OF 41 MEDLINE on STN DUPLICATE 23
91071285. PubMed ID: 2147649. Functional implication for the topographical relationship between MHC class II and the low-affinity IgE receptor: occupancy of CD23 prevents B lymphocytes from stimulating allogeneic mixed lymphocyte responses. Flores-Romo L; Johnson G D; Ghaderi A A; Stanworth D R; Veronesi A; Gordon J. (Department of Immunology, Medical School, Birmingham, GB. ) European journal of immunology, (1990 Nov) 20 (11) 2465-9. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Following the observation of Bonnefoy et al. (J. Exp. Med. 1988. 167:57), that the low-affinity IgE receptor (CD23) on B lymphocytes can be coupled (with the use of chemical cross-linking reagents) to major histocompatibility complex (MHC) class II DR molecules, we now report that ligands binding within the lectin-homology region of CD23 prevent B cells from stimulating allogeneic mixed lymphocyte responses. Ligands capable of blocking mixed lymphocyte responses include the **anti-CD23 antibodies** MHM6 and EBVCS 4 but not EBVCS 1 and 5. IgE itself, and small peptides representing sequences within the CH3 domain of IgE. The detailed topographical relationship between CD23 and MHC class II on the B lymphocyte surface was examined using dual immuno-fluorescence labeling of cells and direct visualization of the staining by confocal laser scanning microscopy. On transformed B lymphoblasts, the two antigens were seen to co-localize in discrete patches; on normal B cells which had been cultured for 2 days with interleukin 4, CD23 and MHC class II converged at a single pole which exhibited a tendency to pseudopod formation and provided a focus for homotypic cell-cell interactions. The possibility that CD23 could serve as a co-stimulatory-adhesion molecule in antigen presentation by B lymphocytes is discussed with special reference to a potential role in the regulation of IgE synthesis.

L6 ANSWER 37 OF 41 MEDLINE on STN DUPLICATE 24
90308277. PubMed ID: 2164062. Monoclonal **anti-CD23 antibodies** induce a rise in [Ca2+]i and polyphosphoinositide hydrolysis in human activated B cells. Involvement of a Gp protein. Kolb J P; Renard D; Dugas B; Genot E; Petit-Koskas E; Sarfati M; Delespesse G; Poggioli J. (U. 196 INSERM Recherche sur les Interferons, Paris, France. ) Journal of immunology (Baltimore, Md. : 1950), (1990 Jul 15) 145 (2) 429-37. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Transduction through the CD23 molecule (Fc epsilon RII) was analyzed in human activated B lymphocytes using **anti-CD23** mAb. B cell blasts expressing an increased amount of surface CD23 molecule were obtained by stimulation of normal peripheral blood B lymphocytes with Staphylococcus aureus strain Cowan I and IL-4. **Anti-CD23** mAb were found to trigger polyphosphoinositide hydrolysis in these cells (and also in tumoral B cells expressing spontaneously CD23) and a rise in [Ca2+]i which could be attributed to mobilization from cytoplasmic pools. This increase in [Ca2+]i could be mimicked, with a comparable time-course, by the addition of InsP3 to permeabilized B cell blasts indicating that the increase in inositol phosphate accumulation induced by the antibodies was due to a preferential attack of phosphatidylinositol-bisphosphate by a specific phosphoinositidase C (PIC). In permeabilized cells, raising the free calcium concentration above 3 microM was found to induce polyphosphoinositides hydrolysis and to activate directly the PIC. Addition of 100 microM GTP-tetralithium salt, a non-hydrolyzable analogue of GTP, also resulted in an increased accumulation of inositol phosphates. A Ca2(+)-dependent PIC, linked to a GTP-binding protein (Gp protein), can thus be activated in B cell blasts. Addition of **anti-CD23 antibodies** to permeabilized B cells in the presence of a physiologic concentration of Ca2+ (100 nM) evoked, within 10 min, a rise in the various inositol phosphates. This ability of **anti-CD23**

**antibodies** to activate PIC was enhanced in the presence of GTP-tetralithium salt 100 microM. By contrast, preincubation with GDP-trilithium salt, a nonhydrolyzable analogue of GDP, caused a marked reduction in the release of inositol phosphates. Preincubation of B cell blasts with Pertussis toxin resulted in a total inhibition of the capacity of the toxin to ADP-ribosylate a 41-kDa protein, probably of the Gi type; in these conditions, no modification of **anti-CD23** -elicited polyphosphoinositide hydrolysis could be detected. These results suggest that the CD23 molecule may be coupled to the phosphoinositide signaling pathway by a GTP-dependent component that is insensitive to Pertussis toxin.

L6 ANSWER 38 OF 41 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

1990:415018 Document No.: PREV199090075819; BA90:75819. HETEROGENEITY IN DIRECT CYTOTOXIC FUNCTION OF L3T4 T CELLS TH1 CLONES EXPRESS HIGHER CYTOTOXIC ACTIVITY TO ANTIGEN-PRESENTING CELLS THAN TH2 CLONES. CHANG J C C [Reprint author]; ZHANG L; EDGERTON T L; KAPLAN A M. IMMUNE RESPONSE CORPORATION, 6455 NANCY RIDGE DRIVE, SAN DIEGO, CALIF 92121, USA. Journal of Immunology, (1990) Vol. 145, No. 2, pp. 409-416.
CODEN: JOIMA3. ISSN: 0022-1767. Language: ENGLISH.

AB In the process of generating culture supernatant from T cell clones, with anti-CD3 antibodies and the B lymphoma A20 as APC, a striking difference in the stimulation of TH1 and TH2 clones was observed, i.e., TH2 clones produced higher levels of lymphokines than TH1 clones. This prompted us to test the hypothesis that differential killing of APC (thus the removal of stimuli) by T cells led to differential T cell activation. By studying a panel of five TH1 and seven TH2 clones, it was demonstrated that TH1 clones mediated significantly higher levels of cytotoxicity toward A20 cells in the presence of soluble anti-CD3 antibody (as opposed to immobilized anti-CE3). Although T cell clones could, when activated with immobilized anti-CD3, produced lymphokines cytotoxic to A20 cells, experiments in which lymphokine production was blocked indicated that T cell clones, in the presence of soluble anti-CD3, mediated killing of A20 through direct cytotoxicity. A higher level of cytotoxicity, by TH1 compared with TH2 clones, was not restricted to anti-CD3 or a partial target cell type, because it also occurred with Con A- or Ag-dependent killing of APC including CH1 (a B lymphoma), RAW 267.4 (a monocyte-macrophage cell line), and LPS blasts. Furthermore, the higher cytotoxic activity of TH1 clones compared with TH2 clones was independent of the stage of T cell activation and was unlikely a result of the length of in vitro culture. High levels of killing of APC led to low levels of T cell activation, the significance of which may be as a negative feedback mechanism in the immune response. Other biologic relevancies of higher cytotoxic activity in TH1 vs TH2 cells were also discussed.

L6 ANSWER 39 OF 41 MEDLINE on STN DUPLICATE 25

87204155. PubMed ID: 3033649. Epstein-Barr virus nuclear antigen 2 specifically induces expression of the B-cell activation antigen CD23. Wang F; Gregory C D; Rowe M; Rickinson A B; Wang D; Birkenbach M; Kikutani H; Kishimoto T; Kieff E. Proceedings of the National Academy of Sciences of the United States of America, (1987 May) 84 (10) 3452-6. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Epstein-Barr virus (EBV) infection of EBV-negative Burkitt lymphoma (BL) cells induces some changes similar to those seen in normal B lymphocytes that have been growth transformed by EBV. The role of individual EBV genes in this process was evaluated by introducing each of the viral genes that are normally expressed in EBV growth-transformed and latently infected lymphoblasts into an EBV-negative BL cell line, using recombinant retrovirus-mediated transfer. Clones of cells were derived that stably express the EBV nuclear antigen 1 (EBNA-1), EBNA-2, EBNA-3, EBNA-leader protein, or EBV latent membrane protein (LMP). These were compared with control clones infected with the retrovirus vector. All 10 clones converted to EBNA-2 expression differed from control clones or clones expressing other EBV proteins by growth in tight clumps and by markedly

increased expression of one particular surface marker of B-cell activation, CD23. Other activation antigens were unaffected by EBNA-2 expression, as were markers already expressed on the parent BL cell line, including BL markers (cALLA and BLA), proliferation markers (transferrin receptor and BK19.9), and cell adhesion-related molecules (LFA-1 and LFA-3). Increased CD23 expression in cells expressing EBNA-2 was apparent from monoclonal **anti-CD23 antibody** binding to the cell surface, from immunoprecipitation of the 45-kDa and 90-kDa CD23 proteins with monoclonal antibody, and from RNA blots probed with labeled CD23 DNA. The results indicate that EBNA-2 is a specific direct or indirect trans-activator of CD23. This establishes a link between an EBV gene and cell gene expression. Since CD23 has been implicated in the transduction of B-cell growth signals, its specific induction by EBNA-2 could be important in EBV induction of B-lymphocyte transformation.

L6 ANSWER 40 OF 41 MEDLINE on STN DUPLICATE 26
87167626. PubMed ID: 2951441. A B cell-specific differentiation antigen, CD23, is a receptor for IgE (Fc epsilon R) on lymphocytes. Yukawa K; Kikutani H; Owaki H; Yamasaki K; Yokota A; Nakamura H; Barsumian E L; Hardy R R; Suemura M; Kishimoto T. Journal of immunology (Baltimore, Md. : 1950), (1987 Apr 15) 138 (8) 2576-80. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Two independent L cell transformants expressing human lymphocyte Fc epsilon R were established by using cellular DNA from RPMI 8866 cells. The surface expression of the receptor was confirmed on the basis of the binding of a panel of anti-Fc epsilon R antibodies and its ability to bind IgE. **Anti-CD23 antibodies** strongly stained the transformants, indicating possible identity or antigenic relationship between Fc epsilon R and CD23. This interesting observation warrants additional clarification as to the role of CD23 and Fc epsilon R in B cell differentiation.

L6 ANSWER 41 OF 41 MEDLINE on STN DUPLICATE 27
87291858. PubMed ID: 3112929. A B cell growth factor-dependent cell line derived from a human lymphocytic nodular lymphoma. Genot E; Kolb J P. Scandinavian journal of immunology, (1987 Jul) 26 (1) 37-46. Journal code: 0323767. ISSN: 0300-9475. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A B cell line derived from a human nodular lymphocytic lymphoma (Brill-Symmers) was shown to be dependent on the presence of a low molecular weight B cell growth factor (BCGF) for its growth in vitro. The caryotype was normal and no contamination with Epstein-Barr virus (EBV) could be detected. These cells did not respond to recombinant gamma interferon or to recombinant human interleukin 2 (IL-2), although they displayed a weak density of IL-2 receptor sites. They were both responsive to and dependent on BCGF for their multiplication in vitro. Furthermore, the putative receptor for this growth factor (CD23) was detected on these cells and the BCGF-dependent proliferation could be blocked by a monoclonal **anti-CD23 antibody.** A tumour-derived cell line like this provides an interesting model for studying the mechanisms regulating B cell growth and the early events leading to the process of B cell immortalization.

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L7            0 L6 AND BINDING AFFINITY

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L8           79 L1 AND AFFINITY

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L10 ANSWER 1 OF 27 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2003:803245 The Genuine Article (R) Number: 719XW. Allergic asthma and an anti-CD23 mAb (IDEC-152): Results of a phase I, singledose, dose-escalating clinical trial. Rosenwasser L J (Reprint); Busse W W; Lizambri R G; Olejnik T A; Totoritis M C. Natl Jewish Med & Res Ctr, Div Clin Immunol & Allergy, 1400 Jackson St, Denver, CO 80206 USA (Reprint); Natl Jewish Med & Res Ctr, Div Clin Immunol & Allergy, Denver, CO 80206 USA; Univ Colorado, Hlth Sci Ctr, Boulder, CO 80309 USA; Univ Wisconsin, Sch Med, Madison, WI USA; Idec Pharmaceut Corp, San Diego, CA USA. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (SEP 2003) Vol. 112, No. 3, pp. 563-570 . Publisher: MOSBY, INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA. ISSN: 0091-6749. Pub. country: USA. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Background: CD23, a cell-surface molecule, is involved in a variety of pathways likely to influence IgE production and inflammation in allergic disorders, such as allergic rhinitis and allergic asthma.

Objective: This study investigated the safety, clinical activity, and pharmacokinetic profile of IDEC-152, an IgG1 anti-**CD23 antibody**, in patients with mild-to-moderate persistent allergic asthma.

Methods: This single-dose, dose-escalating, placebo-controlled study involved 30 patients. Cohorts of 3 to 6 patients received single intravenous infusions of either placebo or IDEC-152 (0.05, 0.25, 1.0, 4.0, 10.0, or 15.0 mg/kg) on study day 1. Safety, clinical activity, and pharmacokinetics were assessed for 12 weeks after treatment.

Results: IDEC-152 was well tolerated. Adverse events (AEs) were mild, no grade 4 or serious AEs were reported, and no relationships were apparent between the dose of IDEC-152 and the frequency, severity, or type of event. The most common AEs in the IDEC-152 group included ecchymosis at the injection site, sinusitis, headache, arthralgia, cold syndrome, infection, throat irritation, and dysmenorrhea. Commonly reported AEs in the placebo group included headache, abdominal pain, and infection. Sustained and dose-dependent decreases in mean IgE concentrations were noted. The mean maximum concentration and area under the curve of IDEC-152 were proportional to the dose administered for the dose range 4.0 to 15.0 mg/kg. The serum half-life of the IDEC-152 antibody increased from 2 to 10 days with increasing doses. After single-dose administration of IDEC-152, no dose-dependent change in FEV1 was observed, and most changes in peak expiratory flow rate were within 10% of baseline values.

Conclusion: These data suggest that IDEC-152 is safe and has the potential for clinical activity in allergic asthma.

L10 ANSWER 2 OF 27 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2004:150247 Document No.: PREV200400146917. Lumiliximab (IDEC-152), an anti-**CD23 antibody**, induces apoptosis in vitro and in vivo in CLL cells. Pathan, Nuzhat [Reprint Author]; Zou, Aihua [Reprint Author]; Wynne, Dee [Reprint Author]; Chu, Peter [Reprint Author]; Thall, Aron [Reprint Author]; Byrd, John; Hanna, Nabil [Reprint Author]; Leigh, Bryan [Reprint Author]. IDEC Pharmaceuticals, San Diego, CA, USA. Blood, (November 16 2003) Vol. 102, No. 11, pp. 438a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB Lumiliximab is a macaque/human chimeric antibody that specifically recognizes CD23, the low **affinity** receptor for IgE on B cells. CD23 is highly upregulated in CLL cells. We have previously established that lumiliximab induces apoptosis in CD23+ B lymphoma cells and in CLL cells (Pathan, et. al., ASH 2001, 2002). Cells from 16 different CLL patients with various levels of disease and treatment histories were

tested for lumiliximab-induced activation of caspase-3. Lumiliximab induced apoptosis in 14/16 CLL patient samples. Lumiliximab-induced apoptosis was associated with cleavage of caspase-3, -9 and PARP, activation of JNK and p38 kinases and downmodulation of anti-apoptotic proteins Mcl-1 and XIAP. Lumiliximab is being tested in a dose-escalating Phase I multicenter clinical trial in CLL patients. Samples were obtained from treated patients and analyzed for in vivo induction of apoptosis in real-time. Patient samples were obtained prior to infusion of lumiliximab and 30 minutes and 2 hours following infusion on Day 1 and Day 2 of treatment. Caspase-3 activation was consistently observed 24 hours after the first infusion and prior to administration of the second infusion. No differences in caspase-3 activation were apparent within two hours after infusion of lumiliximab on Day 1 or Day 2. These data suggest that apoptosis might be a relevant in vivo mechanism of action for lumiliximab in CLL. Lumiliximab also induced decreased expression of Mcl-1 and activation of JNK and p38 kinases on Day 2 following treatment. Additional in vivo pharmacodynamic studies are underway to determine whether lumiximab-induced apoptosis in vivo occurs through similar signaling pathways as that observed in vitro.

L10 ANSWER 3 OF 27 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2004:181248 Document No.: PREV200400181124. Interim results from a phase I study of lumiliximab (IDEC-152, anti-**CD23 antibody**) therapy for relapsed or refractory CLL. Byrd, John C. [Reprint Author]; O'Brien, Susan; Flinn, Ian; Kipps, Thomas J.; Weiss, Mark A.; Reid, Jennifer; Wynne, Dee; Leigh, Bryan R.. Ohio State University, Columbus, OH, USA. Blood, (November 16 2003) Vol. 102, No. 11, pp. 74a. print. Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology. CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB CD23, the low **affinity** IgE receptor, is constitutively expressed on the surface of CLL cells. Lumiliximab is an anti-CD23 monoclonal antibody developed as a macaque-human chimera to minimize immunogenicity. Antitumor activity of lumiliximab was demonstrated in preclinical studies and a clinical study in CLL was initiated. Preliminary data are available from the ongoing, Phase I, dose-escalating, multicenter study assessing the safety, pharmacokinetics, and efficacy of single-agent lumiliximab therapy for relapsed or refractory CLL. Subjects are sequentially assigned to 1 of 6 treatment groups. Therapy consists of IV infusions of lumiliximab over 4 weeks as follows: 125, 250, 375, and 500 mg/m2 once weekly for treatment groups 1,2,3, and 4, respectively; 500 mg/m2 three times per week for Week 1 and 500 mg/m2 once weekly for Weeks 2-4 for treatment group 5; and 500 mg/m2 three times per week for Weeks 1-4 for treatment group 6. Data are available for the first 4 treatment groups (25 subjects). Subjects were predominantly Caucasian (88%) and male (72%), median age 60 years (47 to 79 years), and WHO Performance Status 1 (88%) at study entry. All had progressive CLL after a median of 3 prior treatment regimens (1 to 12 prior treatment regimens); 52% were fludarabine-refractory and 52% were Rai stage III/IV. Antibody infusions were administered in an outpatient setting and were well tolerated. A total of 69 study-related adverse events (probable, possible, or unknown relationship to study treatment) were reported in 16 of 25 (64%) subjects. The most common study-related adverse events were fatigue, nausea, headache, cough, and increased sweating. Two of 10 subjects in treatment group 4 had dose-limiting toxicities: Grade 4 neutropenia possibly related to treatment and Grade 4 headache probably related to treatment. Absolute lymphocyte count (ALC) reductions were observed in all treatment groups (24 of 25 subjects), with a gtoreq50% ALC decrease in 8 of 19 (42%) subjects enrolled in treatment groups 3 and 4. Reductions in lymphadenopathy were also observed. These results suggest that lumiliximab can be administered safely and may have clinical activity in subjects with heavily pretreated CLL. Accrual and response evaluations are ongoing.

L10 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
2002:483084 Document No. 137:62139 Canine low **affinity** IgE receptor (CD23), nucleic acid molecules and antibodies for identifying regulatory compounds and diagnosing and treating allergic diseases. Weber, Eric R.; McCall, Catherine A. (Heska Corporation, USA). U.S. US 6410714 B1 20020625, 33 pp. (English). CODEN: USXXAM. APPLICATION: US 2000-535521 20000324. PRIORITY: US 1999-PV125913 19990324.

AB The present invention relates to canine low **affinity** IgE receptor (CD23) nucleic acid mols., proteins encoded by such nucleic acid mols., antibodies raised against such proteins, compds. capable of regulating, e.g., inhibiting or activating, the function of such proteins, and methods to identify such regulatory compds. The present invention also includes therapeutic compns. comprising such nucleic acid mols., proteins, antibodies, or regulatory compds., methods to use such therapeutic compns., and methods and kits to detect CD23 proteins. The CD23 polypeptides, encoding polynucleotides and antibodies are useful for treating allergic diseases such as atopic dermatitis, asthma, inflammation, hay fever, and food sensitivities.

L10 ANSWER 5 OF 27 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2002:316992 The Genuine Article (R) Number: 538KE. Anti-CD23 monoclonal antibody inhibits germline C epsilon transcription in B cells. Yabuuchi S (Reprint); Nakamura T; Kloetzer W S; Reff M E. Seikagaku Corp, Cent Res Labs, 1253 Tateno 3 Chome, Tokyo 2070021, Japan (Reprint); Seikagaku Corp, Cent Res Labs, Tokyo 2070021, Japan; Chiba Univ, Grad Sch Med, Dept Mol Immunol, Chuo Ku, Chiba 2608670, Japan; IDEC Pharmaceut Corp, San Diego, CA 92121 USA. INTERNATIONAL IMMUNOPHARMACOLOGY (MAR 2002) Vol. 2, No. 4, pp. 453-461. Publisher: ELSEVIER SCIENCE BV. PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 1567-5769. Pub. country: Japan; USA. Language: English.
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB A chimeric macaque/human (PRIMATIZED(R)) anti-**CD23 antibody**, p6G5G1, demonstrated a strong inhibitory effect on IL-4-and anti-CD40 antibody-stimulated IgE production by human peripheral blood mononuclear cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE through the inhibition of germline Cepsilon RNA synthesis. Early addition of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE inhibition. In contrast, later addition of p6G5G1 still showed inhibition of increased levels of surface CD23, which is normally upregulated by stimulation with IL-4 and anti-CD40. (C) 2002 Published by Elsevier Science B.V.

L10 ANSWER 6 OF 27 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2002:223261 Document No.: PREV200200223261. Inhibition of B-cell activation by delta(9)-tetrahydrocannabinol. Wallace, D. J. [Reprint author]; Quashne, R. [Reprint author]; Ryan, J. J.; Fischer-Stenger, K. J. [Reprint author]. University of Richmond, Richmond, VA, USA. Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 353. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society of Microbiology.
ISSN: 1060-2011. Language: English.

AB Delta9-tetrahydrocannabinol (THC) is known as the major psychoactive component of marijuana and it is now clear that cannabinoids and cannabinoid-related molecules are also involved in immune regulation. By binding to cannabinoid-specific receptors, these molecules have been shown to decrease the proliferation of lymphocytes and reduce antibody production by B-lymphocytes. However, the mechanisms responsible for these effects are not clearly understood. Interleukin-4 (IL-4) is a

pleiotropic cytokine produced by TH2-cells that is known to induce the proliferation of B-lymphocytes and induce antibody production by these cells. IL-4 has also been shown to increase the expression of CD23 (low **affinity** IgE receptor) on the surface of B-cells. Therefore, the expression of CD23 can be used as a marker for B-cell activation. The purpose of this study was to determine whether THC inhibits B-cell activation induced by IL-4 stimulation. The M-12 murine B-cell line and the WIL-2 human B-cell line were plated in 96-well microtiter plates (4X104 cells/well) and incubated in the presence of THC (0.01-10 muM) and simultaneously stimulated with IL-4 (0.5-5 ng/ml) for 24 to 48 hours. The cells were then stained with FITC-labeled anti-**CD23 antibody** and analyzed by flow cytometry to detect the expression of CD23 on the surface of the B-cells. These studies demonstrated that triggering with 5 ng/ml of IL-4 for 48 hours induced peak levels of CD23 expression on the B-cells. Exposure to THC downregulated the expression of CD23 on murine B-cells (mean fluorescence intensity: 34 with IL-4 alone, 14 with IL-4 and THC) and to a lesser degree on human B-cells (mean fluorescence intensity: 65 with IL-4 alone, 48 with IL-4 and THC). These results suggest that THC inhibits B-cell activation induced by IL-4 stimulation which may be responsible for the drug-induced decrease in antibody production observed in B-lymphocytes.

L10 ANSWER 7 OF 27 MEDLINE on STN DUPLICATE 1

2001403419. PubMed ID: 11454061. Endocytosis and recycling of the complex between CD23 and HLA-DR in human B cells. Karagiannis S N; Warrack J K; Jennings K H; Murdock P R; Christie G; Moulder K; Sutton B J; Gould H J. (The Randall Centre for Molecular Mechanisms of Cell Function, King's College London, UK.. hjg@helios.rai.kcl.ac.uk) . Immunology, (2001 Jul) 103 (3) 319-31. Journal code: 0374672. ISSN: 0019-2805. Pub. country: England: United Kingdom. Language: English.

AB The presentation of extremely low doses of antigen to T cells is enhanced by immunoglobulin E (IgE)-dependent antigen focusing to CD23, the low-**affinity** receptor for IgE, expressed on activated B cells. CD23 contains a C-type lectin domain in its extracellular sequence and a targeting signal for coated pits, required for endocytosis, in its cytoplasmic sequence. CD23 is non-covalently associated with the major histocompatibility complex class II antigen, human leucocyte antigen HLA-DR, on the surface of human B cells, but the fate of this complex following endocytosis is unknown. To answer this question we have labelled these proteins on the surface of RPMI 8866 B cells and traced their route through the cytoplasm. Endocytosis mediated by anti-**CD23 antibodies** (BU38 and MHM6) led to the loss of CD23 from the cells. Endocytosis mediated by an antibody to HLA-DR (CR3/43) or an antigen-IgE complex (NP-BSA-anti-NP IgE), however, led to recycling of the HLA-DR-CD23 complex to the cell surface on a time scale (3-6 hr) consistent with the recycling of HLA-DR in antigen presentation. Along the latter pathway CD23 label was observed in cytoplasmic organelles that resembled the 'compartments for peptide loading' or 'class II vesicles' described by previous authors. Two features of the recycling process may contribute to the efficiency of antigen presentation. Peptide exchange may be facilitated by the proximity of HLA-DR and antigen in peptide loading compartments of the endosomal network. The return of CD23 with HLA-DR to the cell surface may then help to stabilize specific B-cell-T-cell interactions, contributing to T-cell activation.

L10 ANSWER 8 OF 27 MEDLINE on STN DUPLICATE 2

2001015588. PubMed ID: 11018076. Enhanced intestinal transepithelial antigen transport in allergic rats is mediated by IgE and CD23 (FcepsilonRII). Yang P C; Berin M C; Yu L C; Conrad D H; Perdue M H. (Intestinal Disease Research Program and Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada. ) Journal of clinical investigation, (2000 Oct) 106 (7) 879-86. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB We previously reported that active sensitization of rats resulted in the

appearance of a unique system for rapid and specific antigen uptake across intestinal epithelial cells. The current studies used rats sensitized to horseradish peroxidase (HRP) to define the essential components of this antigen transport system. Sensitization of rats to HRP stimulated increased HRP uptake into enterocytes (significantly larger area of HRP-containing endosomes) and more rapid transcellular transport compared with rats sensitized to an irrelevant protein or naive control rats. Whole serum but not IgE-depleted serum from sensitized rats was able to transfer the enhanced antigen transport phenomenon. Immunohistochemistry demonstrated that sensitization induced expression of CD23, the low-**affinity** IgE receptor (FcepsilonRII), on epithelial cells. The number of immunogold-labeled CD23 receptors on the enterocyte microvillous membrane was significantly increased in sensitized rats and was subsequently reduced after antigen challenge when CD23 and HRP were localized within the same endosomes. Finally, pretreatment of tissues with luminally added anti-**CD23 antibody** significantly inhibited both antigen transport and the hypersensitivity reaction. Our results provide evidence that IgE antibodies bound to low-**affinity** receptors on epithelial cells are responsible for the specific and rapid nature of this novel antigen transport system.

L10 ANSWER 9 OF 27 MEDLINE on STN DUPLICATE 3
2000150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan. ) International journal of immunopharmacology, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low **affinity** receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) monoclonal antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23 antibody** in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23 antibodies** inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

L10 ANSWER 10 OF 27 MEDLINE on STN DUPLICATE 4
1999135997. PubMed ID: 9949321. Production of chemokines and proinflammatory and antiinflammatory cytokines by human alveolar macrophages activated by IgE receptors. Gosset P; Tillie-Leblond I; Oudin S; Parmentier O; Wallaert B; Joseph M; Tonnel A B. (Unite INSERM U416, Institut Pasteur, Lille, France. ) Journal of allergy and clinical immunology, (1999 Feb) 103 (2 Pt 1) 289-97. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: The alveolar macrophage (AM) expresses the low **affinity** IgE receptor and has the ability to produce not only several proinflammatory cytokines (TNF-alpha, IL-1, IL-6) but also

antiinflammatory cytokines (IL-1 receptor antagonist [IL-1ra], IL-10), chemokines (IL-8, monocyte chemotactic protein-1 [MCP-1]), and macrophage inflammatory protein-1alpha (MIP-1alpha). OBJECTIVE: The aim of this study was to evaluate the capacity of the AM from patients with allergic asthma and control subjects to produce chemokines and antiinflammatory versus proinflammatory cytokines after activation by IgE receptors and to define the role of CD23 in this activation. METHODS: AMs were collected by bronchoalveolar lavage from 13 patients with allergic asthma and 14 healthy subjects. Adherent AMs were activated either by the successive addition of IgE and anti-IgE or by monoclonal mouse IgG anti-CD23 or by a control monoclonal mouse antibody. TNF, IL-1beta, IL-1ra, IL-10, IL-8, MCP-1, and MIP-1alpha levels were evaluated in supernatants of AMs incubated for 18 hours and in some cases after 4 hours of incubation. RESULTS: Activation by IgE and anti-IgE antibodies significantly increased the production of TNF, IL-1beta, IL-8, MCP-1, MIP-1alpha, and IL-10 in both control subjects and patients with asthma, whereas the increase for IL-1ra was only significant for the control subjects. Whereas F(ab) fragments of anti-**CD23 antibodies** inhibited IgE plus anti-IgE-induced cytokine production, activation by monoclonal IgG anti-**CD23 antibodies** reproduced the effect of IgE immune complexes. At 4 hours, the secretion of proinflammatory cytokines was increased by activation by IgE receptors, in contrast to antiinflammatory cytokines. In addition, analysis of the balance between proinflammatory and antiinflammatory cytokines showed that IgE-dependent activation largely favored the proinflammatory cytokines, particularly in patients with asthma. CONCLUSION: IgE-dependent activation by the FcepsilonRII receptor upregulates the synthesis of both chemokines and antiinflammatory cytokines in addition to proinflammatory cytokines. However, AMs from patients with allergic asthma may promote airway inflammation after activation by IgE receptors through its preferential effect on proinflammatory cytokines.

L10 ANSWER 11 OF 27 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

1999:1848 Document No.: PREV199900001848. Binding of anti-CD23 monoclonal antibody to the leucine zipper motif of FcepsilonRII/CD23 on B cell membrane promotes its proteolytic cleavage. Evidence for an effect on the oligomer/monomer equilibrium. Munoz, Olivier; Brignone, Chrystelle; Grenier-Brossette, Nicole; Bonnefoy, Jean-Yves; Cousin, Jean-Louis [Reprint author]. INSERM U343, Hopital de l'Archet, B.P. 79, F-06202 Nice cedex 03, France. Journal of Biological Chemistry, (Nov. 27, 1998) Vol. 273, No. 48, pp. 31795-31800. print.
CODEN: JBCHA3. ISSN: 0021-9258. Language: English.

AB In the present study we have compared the binding of two monoclonal antibodies to CD23, EBVCS1 and mAb25, which recognize the stalk and the lectin domain, respectively, on the CD23 molecule. At 4degreeC, EBVCS1 binds to about 10% of the receptors recognized by mAb25 on the B cell surface. At 37degreeC, whereas mAb25 reaches its maximal binding within a few seconds, EBVCS1 requires 60 min to bind to the same extent. Stabilization of the oligomeric structure of CD23 with IgE strongly affects in a dose-dependent fashion the number of binding sites seen by EBVCS1 but not the t1/2 to reach them, suggesting that EBVCS1 binds to the coiled coil region through an allosteric mechanism. EBVCS1 rapidly down-modulates the membrane CD23 expression with a coincident increase of CD23-soluble fragments in the culture medium, an effect that is inhibited by IgE. In contrast, mAb25, as well as IgE, protects CD23 from proteolytic cleavage and stimulates its endocytosis. These results suggest that EBVCS1 unravels the coiled coil structure of CD23, rendering it more susceptible to proteolytic attack. This supports the oligomeric model proposed previously (Gould, H., Sutton, B., Edmeades, R., and Beavil, A. (1991) Monogr. Allergy 29, 28-49). The biological significance of these observations is discussed.

L10 ANSWER 12 OF 27 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 5

1997:415432 Document No.: PREV199799707475. Involvement of both protein kinase C and G proteins in superoxide production after IgE triggering in guinea pig eosinophils. Aizawa, Toshiya [Reprint author]; Tamura, Gen; Sanpei, Ken-Ichi; Shibasaki, Atsushi; Shirato, Kunio; Takishima, Tamotsu. Fukushima Cent. Hosp., Yoshikura Aza Yachi 52, Fukushima City 960, Japan. Allergology International, (1997) Vol. 46, No. 2, pp. 91-99. ISSN: 1323-8930. Language: English.

AB To study the function and mechanism of eosinophils via the low **affinity** IgE receptor (FC-epsilon-RII), we examined the production of O-2 metabolites by measuring the luminol-dependent chemiluminescence (LDCL) response and the generation of cysteinyl leukotrienes. Eosinophils obtained from guinea pig peritoneal fluid sensitized with horse serum were purified. Luminol-dependent chemiluminescence was induced by stimulation with monoclonal anti-**CD23 antibody**, but not by mouse serum (controls). The mean (+-SEM) value of LDCL was 20.6+-1.3 times 10-3c.p.m. This reaction consisted of an initial rapid phase and a propagation phase and ended within 10min. Guinea pig eosinophils were histochemically stained with monoclonal anti-**CD23 antibody.** The major product generated in the LDCL response was superoxide, as determined by the measurement of superoxide by cytochrome c reduction and the complete inhibitory effect of superoxide dismutase on the LDCL response. Pretreatment with either pertussis toxin or cholera toxin inhibited the LDCL reaction. Depletion of bivalent ions by EDTA inhibited this response and the protein kinase C inhibitor D-Sphingosin inhibited both 1-oleoyl-2acetyl-glycerol-induced and FC-epsilon-RII-mediated LDCL. These findings suggest that the NADPH-protein kinase C pathway may be involved in the Fc-epsilon-RII-mediated LDCL response in guinea pig eosinophils.

L10 ANSWER 13 OF 27 MEDLINE on STN DUPLICATE 6

97032129. PubMed ID: 8878025. Use of CD23 (BU38) on paraffin sections in the diagnosis of small lymphocytic lymphoma and mantle cell lymphoma. Kumar S; Green G A; Teruya-Feldstein J; Raffeld M; Jaffe E S. (Hematopathology Section, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892-1500, USA. ) Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc, (1996 Sep) 9 (9) 925-9. Journal code: 8806605. ISSN: 0893-3952. Pub. country: United States. Language: English.

AB The CD23 antigen is a low-**affinity** immunoglubulin E receptor that is expressed during B-cell activation. Recently, it has been shown to be of diagnostic utility in distinguishing between small lymphocytic lymphoma (SLL) and mantle cell lymphoma (MCL), two entities that can have similar morphologic and immunophenotypic features. Such studies, however, generally required viable cells in cell suspension or cryostat sections for detection of CD23. We evaluated staining for the CD23 antigen in paraffin sections, using BU38, an antibody that detects a fixation-resistant epitope of the antigen. We analyzed 44 SLLs, 3 lymphoplasmacytoid lymphomas, and 39 MCLs. Staining was performed on formalin- or B5-fixed paraffin-embedded tissue sections using L26 (CD20), CD3, Leu22 (CD43), and BU38 (**CD23**) **antibodies.** All of the cases were of B-cell phenotype (CD20+), and 42/44 SLLs, 3/3 lymphoplasmacytoid lymphomas, and 33/39 MCLs coexpressed the CD43 antigen. CD23 was positive in 41 (93%) of 44 SLLs. The majority of neoplastic cells (75% or more) stained positively, with a membranous pattern of staining. The staining was moderate in intensity and easily interpreted. Only 1/39 MCLs and 1/3 lymphoplasmacytoid lymphomas were CD23 positive. CD23-positive follicular dendritic cells were, however, present in all of the MCLs, either in residual follicles or in large, disordered meshworks. These results demonstrate that the BU38 antibody can detect CD23 on the cells of SLLs in paraffin sections and that this antibody can have diagnostic utility in routine diagnosis.

L10 ANSWER 14 OF 27 MEDLINE on STN DUPLICATE 7

96071560. PubMed ID: 7585180. Marked amelioration of established collagen-induced arthritis by treatment with antibodies to CD23 in vivo.

Plater-Zyberk C; Bonnefoy J Y. (Glaxo Institute for Molecular Biology, Immunology Department, Geneva, Switzerland. ) Nature medicine, (1995 Aug) 1 (8) 781-5. Journal code: 9502015. ISSN: 1078-8956. Pub. country: United States. Language: English.

AB CD23 is a low-**affinity** receptor for immunoglobulin E (IgE) expressed by a variety of haematopoietic cells. Proteolytic cleavage of the transmembrane receptor generates soluble forms, which can be detected in biological fluids. CD23 regulates many functional aspects of immune cells, both in its cell-associated and soluble forms. In view of the increased levels of CD23 in rheumatoid arthritis, we have studied the effect of neutralizing CD23 in type II collagen-induced arthritis in mice, a model for human rheumatoid arthritis. Successful disease modulation is achieved by treatment of arthritic DBA/1 mice with either polyclonal or monoclonal antibodies to mouse CD23. Treated mice show a dose-related amelioration of arthritis with significantly reduced clinical scores and number of affected paws. This improvement in clinical severity is confirmed by histological examination of the arthritic paws. A marked decrease in cellular infiltration of the synovial sublining layer and limited destruction of cartilage and bone is evident in animals treated with therapeutic doses of anti-**CD23 antibody.** These findings demonstrate the involvement of CD23 in a mouse model of human rheumatoid arthritis.

L10 ANSWER 15 OF 27 MEDLINE on STN DUPLICATE 8

96098157. PubMed ID: 7503406. An enzyme-linked immunosorbent assay specific for transient (29-37-kDa) fragments of soluble CD23/IgE-binding factors. Katira A; Gordon J. (Department of Immunology, Medical School, Birmingham, UK. ) Allergy, (1995 Aug) 50 (8) 689-92. Journal code: 7804028. ISSN: 0105-4538. Pub. country: Denmark. Language: English.

AB The low-**affinity** IgE receptor (Fc epsilon RII) of B cells and monocytes--also known as CD23--is released from the cell surface by proteolytic cleavage to yield a series of soluble fragments which can accumulate in cell culture supernatants and body fluids. Of these, the most stable is a 25-kDa molecule which is generated from transient intermediates ranging in size from 29 to 37 kDa. It has been claimed that these latter species act as IgE-promoting factors while the 25-kDa molecule is endowed with various cytokine-like activities which are independent of IgE binding. We describe here a novel enzyme-linked immunosorbent assay (ELISA) which allows for the distinction between these two classes of soluble CD23. It is based on the observation that the **CD23 antibody** EBVCS1 can capture recombinant 29-kDa and 37-kDa fragments of CD23 but does not bind to the 25-kDa species: when EBVCS5 is used as the capture antibody, all three fragments are bound. The availability of these differential ELISA should facilitate investigations on the biological properties of CD23 fragments in health and disease.

L10 ANSWER 16 OF 27 MEDLINE on STN DUPLICATE 9

95317800. PubMed ID: 7797246. Functional significance of CD23- on CD23-transfected Th2 clone. Nambu M; Hagen M; Sandor M; Sacco R E; Kwack K; Lynch R G. (Department of Pathology, College of Medicine, University of Iowa, Iowa City 52242, USA. ) Immunology letters, (1995 Jan) 44 (2-3) 163-7. Journal code: 7910006. ISSN: 0165-2478. Pub. country: Netherlands. Language: English.

AB CD23, a low-**affinity** IgE Fc receptor, is not displayed on most resting T cells but its expression has been shown to be transiently induced in vivo and in vitro on some CD4+ T cells [1-4] and in vivo on CD8+ T cells by IgE-secreting hybridoma tumors [5]. To investigate the functional role of CD23 on T cells, we inserted a CD23 construct into an expression vector driven by a CD2 promoter and transfected it into a murine Th2 clone D10.G4.1 (D10). We stimulated the transfected D10 cells (D10.3M.24) with anti-TCR antibody in the presence or absence of IgE, and measured IL-4, IL-5 and IL-6 production in the culture supernatants. Activation of D10.3M.24 cells by anti-TCR antibody induced greater levels of IL-4, IL-5 and IL-6 production, when the TCR and CD23 were

co-crosslinked by TNP anti-TCR and IgE anti-TNP antibodies. IgG anti-TNP antibody did not enhance lymphokine production by D10.3M.24 cells. The enhanced lymphokine production by IgE was blocked by monoclonal anti-**CD23 antibody.** IgE anti-TNP antibody did not enhance lymphokine production by the wild-type D10 cells induced by TNP anti-TCR antibody. These studies show that when co-crosslinked with the TCR, CD23 can modulate the lymphokine production in activated Th2 cells. Since CD23 binds to IgE and also binds to CD21 [6], a complement receptor commonly expressed on B cells, T-cell CD23 could play an immunoregulatory role during cognate T-B cell interaction and during IgE antibody responses.

L10 ANSWER 17 OF 27 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

95:236073 The Genuine Article (R) Number: QN916. DEVELOPMENTAL REGULATION OF FC-EPSILON-RII/CD23 EXPRESSION IN B-LINEAGE CELLS - EVIDENCE FOR TRANSCRIPTIONAL AND POSTTRANSCRIPTIONAL LEVELS OF CONTROL. HAGEN M (Reprint); SANDOR M; LYNCH R G. UNIV IOWA, COLL MED, DEPT PATHOL, MRC 375, IOWA CITY, IA, 52242 (Reprint). IMMUNOLOGY LETTERS (JAN 1995) Vol. 44, No. 2-3, pp. 157-162. ISSN: 0165-2478. Pub. country: USA. Language: ENGLISH. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The present studies show that the expression of cell surface Fc epsilon RII/CD23, detected with the monoclonal anti-Fc epsilon RII/**CD23 antibody** B3B4 or by the binding of IgE, is not restricted to the stage of resting mature virgin B lymphocytes. Murine CD23 was detected as a cell surface protein on two sIgG(+) B-cell lines. Moreover, we detected full-length transcripts for Fc epsilon RII/CD23 in several members of a panel murine B lymphoid lineage cell lines representative of all stages of murine B lymphocyte development. Our findings suggest that regulation of CD23 translation may differ between B-cell lines at various stages of differentiation. The detection of mRNA transcripts for Fc epsilon RII/CD23 was not restricted to transformed cell lines. Fc epsilon RII/CD23 transcripts were amplified by RT-PCR from peritoneal and splenic B lymphocyte subpopulations that were sorted by flow cytometry into populations that did not express surface Fc epsilon RII/CD23. Our findings suggest that Fc epsilon RII/CD23 transcription and translation are not necessarily restricted to the narrow developmental window of murine B lymphocyte differentiation as previously thought. Our findings imply that Fc epsilon RII/CD23 may be expressed at the protein level at various stages of murine B lymphocyte differentiation. Investigations into the expression patterns and potential mechanisms of regulation of Fc epsilon RII/CD23 could provide insight into the basis for the wide range of immunological functions that have been proposed for Fc epsilon RII/CD23.

L10 ANSWER 18 OF 27 MEDLINE on STN DUPLICATE 10

96159495. PubMed ID: 8589271. Involvement of CD23/Fc epsilon RII in the homotypic and heterotypic cytoadhesion of the human eosinophilic cell line Eol-3. Yamaoka K A; Kolb J P. (U 365 INSERM, Interferons et Cytokines, Institut Curie, Paris, France. ) European cytokine network, (1995 May-Jun) 6 (3) 145-55. Journal code: 9100879. ISSN: 1148-5493. Pub. country: France. Language: English.

AB A subclone of the EoL-3 human eosinophilic leukemia cell line (EoL-3.12) was selected for its high inducibility of CD23 (low **affinity** IgE receptor/Fc epsilon RII) by IL-4. Maximum membrane CD23 expression was detected after 16 h of incubation with IL-4, then gradually returned to basal level after 48 h. Membrane expression of CD23 on EoL-3.12 cells was found to parallel their homotypic aggregation. Extending the time of incubation with IL-4 to 48 h or more resulted in a de-aggregation of cells of cells with a shedding of membrane CD23 and an increase of its soluble form, sCD23. The IL-4-induced aggregation of EoL-3.12 cells was inhibited with anti-**CD23 antibody** or human myeloma IgE protein, indicating that it was mediated through the engagement of CD23. EoL3.12 incubated with IL-4 displayed morphological changes associated with differentiation, such as an increased number of lobulated nuclei with prominent nucleoli, increased ratio of cytoplasm and distinct cytoplasmic processes. EoL-3.12 cells incubated with IL-4 also displayed an enhanced

adherence to human umbilical vein endothelial cells (HUVEC), which was reverted when the IL-4 incubation time extended. Furthermore, the transendothelial migration of EoL-3.12 cells toward a chemokinetic gradient of soluble CD23 (sCD23; 29 kDa fragment) closely paralleled the density of membrane CD23 expressed on EoL-3.12 cells. Additionally, the engagement of CD23 led to the activation of the L-arginine-dependent pathway of nitric oxide (NO) production, as detected by the increase in intracytoplasmic cGMP concentration. The capacity of EoL-3.12 cells to form homotypic as well as heterotypic adhesion appears therefore to be regulated, at least in part, by the level of CD23 expression.

L10 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
1994:296620 Document No. 120:296620 Induction of B cell and T cell tolerance in vivo by anti-CD23 mAb. Morris, Suzanne C.; Lees, Andrew; Holmes, Joanne M.; Jeffries, Ramona D. A.; Finkelman, Fred D. (Dep. Med., Uniformed Serv. Univ. Health Sci., Bethesda, MD, 20814, USA). Journal of Immunology, 152(8), 3768-76 (English) 1994. CODEN: JOIMA3. ISSN: 0022-1767.
AB T cell tolerance can be induced by B cell presentation of Ags to naive T cells. To further characterize this mechanism of T cell tolerance induction, the authors have investigated the effects of injecting mice with an intact rat IgG2a Ab, which binds to the B cell low-**affinity** Fcε receptor (CD23), on the responsiveness of B cells and T cells to rat IgG2a. The authors' observations indicate that (1) i.v., s.c., or i.p. injection of this Ab induces antigen-specific B cell and T cell tolerance; (2) both forms of tolerance are induced more completely by injection of rat IgG2a anti-CD23 mAb than by injection of an equal dose of a control rat IgG2a Ig; and (3) reduced responsiveness to Ag is seen as early as 1-3 days after anti-CD23 mAb injection and reaches maximum levels by 7 days after injection. Although tolerance induced by the injection of soluble proteins has been reported to be characterized by reduced production of IL-2 and IFN-γ, but normal production of IL-4, injection of mice with rat IgG2a anti-mouse CD23 mAb greatly decreases the IL-4 response to a rat IgG2a immunogen that normally induces a large IL-4 response.

L10 ANSWER 20 OF 27 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 11
91:364397 The Genuine Article (R) Number: FT273. IGE AND SWITCHING PHENOMENA. BONNEFOY J Y (Reprint). GLAXO INST MOLEC BIOL, CHEMIN AULX, CH-1228 PLAN LES OUATES, SWITZERLAND (Reprint). SEMAINE DES HOPITAUX (1991) Vol. 67, No. 26-2, pp. 1199-1200. Pub. country: SWITZERLAND. Language: French. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB In allergic disorders, IgE increases following allergen stimulation. In vitro IgE synthesis is the result of a complex interaction between T-cells, B-cells and monocytes, controlled by cytokines produced by T-cells and monocytes (IL-4, IL-5, IFN-gamma, and IL-6). IL-4 acts as a switching factor to induce synthesis of IgE. IFN-gamma inhibits IL-4 induced IgE synthesis. IL-4 is a mastocyte growth factor, as well as IL-3. Moreover, IL-4 is a potent inducer of FceR/CD23 expression of B-cells and monocytes. Monoclonal anti-**CD23 antibodies** inhibit IL-4-induced IgE synthesis in an isotype-specific manner. IL-4-producing T-cells also produce IL-5 which induces differentiation of eosinophil precursors. Eosinophils, in turn, express low **affinity** receptors for IgE when activated. Activation of the IgE system thus leads to increased IgE production and increased expression of IgE receptors. This results in increased receptor-ligand interactions, resulting in release of numerous chemical mediators involved in the pathogenesis of allergic disorders.

L10 ANSWER 21 OF 27 MEDLINE on STN DUPLICATE 12
91071285. PubMed ID: 2147649. Functional implication for the topographical relationship between MHC class II and the low-**affinity** IgE receptor: occupancy of CD23 prevents B lymphocytes from stimulating allogeneic mixed lymphocyte responses. Flores-Romo L; Johnson G D; Ghaderi

A A; Stanworth D R; Veronesi A; Gordon J. (Department of Immunology, Medical School, Birmingham, GB. ) European journal of immunology, (1990 Nov) 20 (11) 2465-9. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Following the observation of Bonnefoy et al. (J. Exp. Med. 1988. 167:57), that the low-**affinity** IgE receptor (CD23) on B lymphocytes can be coupled (with the use of chemical cross-linking reagents) to major histocompatibility complex (MHC) class II DR molecules, we now report that ligands binding within the lectin-homology region of CD23 prevent B cells from stimulating allogeneic mixed lymphocyte responses. Ligands capable of blocking mixed lymphocyte responses include the anti-**CD23 antibodies** MHM6 and EBVCS 4 but not EBVCS 1 and 5. IgE itself, and small peptides representing sequences within the CH3 domain of IgE. The detailed topographical relationship between CD23 and MHC class II on the B lymphocyte surface was examined using dual immuno-fluorescence labeling of cells and direct visualization of the staining by confocal laser scanning microscopy. On transformed B lymphoblasts, the two antigens were seen to co-localize in discrete patches; on normal B cells which had been cultured for 2 days with interleukin 4, CD23 and MHC class II converged at a single pole which exhibited a tendency to pseudopod formation and provided a focus for homotypic cell-cell interactions. The possibility that CD23 could serve as a co-stimulatory-adhesion molecule in antigen presentation by B lymphocytes is discussed with special reference to a potential role in the regulation of IgE synthesis.

L10 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

1991:605371 Document No. 115:205371 Signalling pathway through the CD23 molecule in human B cells. Kolb, J. P.; Dugas, B.; Renard, D.; Genot, E.; Poggioli, J.; Delespesse, G. (Inst. Curie, Paris, Fr.). Advances in Prostaglandin, Thromboxane, and Leukotriene Research, 21B(Prostaglandins Relat. Compd.), 997-1004 (English) 1990. CODEN: ATLRD6. ISSN: 0732-8141.

AB Incubation of human activated B-cells with monoclonal antibodies to antigen CD23 (a low-**affinity** IgE receptor) induced hydrolysis of polyphosphoinositide (catalyzed by phosphoinositidase C) and an increase in intracellular Ca2+ concentration This treatment caused crosslinking of CD23-bound IgE. The activation of phosphoinositidase C involved a pertussis toxin-insensitive GTP-binding protein.

L10 ANSWER 23 OF 27 MEDLINE on STN DUPLICATE 13

90361973. PubMed ID: 2144015. Thromboxane release by lymphokine-differentiated U937 human monocytic cells: response to platelet-activating factor (PAF) and chemotactic peptide (FMLP) but not to low **affinity** IGE-receptor (Fc epsilon RII/CD23) occupation. Storch J; Edwards R J; MacDermot J. (Department of Clinical Pharmacology, Royal Postgraduate Medical School, London. ) Journal of leukocyte biology, (1990 Sep) 48 (3) 266-73. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB The primary objective of this study was to explore if the CD23 antigen is a functional low **affinity** IgE receptor on macrophages for the release of thromboxane B2 (TXB2). The responsiveness of U937 monocytic cells and their macrophage-like inducible forms to platelet-activating factor (Paf), the chemotactic peptide fMLP, and low **affinity** IgE-receptor occupation was examined. Differentiation of U937 cells by phorbol myristate acetate (PMA) and a cancer cell line (HBT 5637) conditioned medium (5637-CM), but not INFg or IL4, resulted in a macrophage-like cell line which released TXB2. A high basal release of TXB2 with no significant response to Paf or fMLP challenge was seen following culture of cells with PMA. In 5637-CM-differentiated cells, Paf and fMLP induced a rapid release of TXB2, about 10 fold above basal activity. There was a slow Ca-independent response to short-term treatment with PMA and a rapid Ca-dependent response to the ionophore A23187. Both stimulants acted synergistically on TXB2 synthesis in 5637-CM differentiated cells. Although low **affinity** receptors for IgE (Fc epsilon RII/CD23) were induced by 5637-CM, no TXB2 was

released in response to soluble or latex-bound IgE-antigen complexes or to anti-Fc epsilon RII/**CD23-antibodies.** IL4 and to a lesser extent INFg both induced Fc epsilon RII/CD23 receptor expression, but inhibited release of TXB2 in response to Paf, fMLP, or PMA. We conclude that the functional receptors for IgE on mature macrophages are most probably not Fc epsilon RII/CD23.

L10 ANSWER 24 OF 27 MEDLINE on STN DUPLICATE 14
89358095. PubMed ID: 2527805. Soluble fragments of the low-**affinity** IgE receptor (CD23) inhibit the spontaneous migration of U937 monocytic cells: neutralization of MIF-activity by a **CD23 antibody.** Flores-Romo L; Cairns J A; Millsum M J; Gordon J. (Department of Immunology, University of Birmingham, U.K. ) Immunology, (1989 Aug) 67 (4) 547-9. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.
AB U937 monocytic cells were found to respond by diminished spontaneous migration when confronted with **affinity**-purified soluble fragments of the low-**affinity** receptor for IgE (FcER2/CD23). Unlike B lymphoma cells, U937 cells could not be activated to respond with enhanced DNA synthesis through their membrane-bound CD23 antigen by MHM6, a monoclonal antibody within the CD23 cluster. MHM6 did, however, effectively neutralize the U937-directed MIF (migration inhibition factor) activity contained within the soluble CD23 preparations. The findings not only suggest a role for soluble CD23 as a novel cytokine at sites of inflammation but also indicate different functions for the membrane-bound forms expressed on B cells and monocytes.

L10 ANSWER 25 OF 27 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
89:413607 The Genuine Article (R) Number: AJ341. SOLUBLE FRAGMENTS OF THE LOW-**AFFINITY** IGE RECEPTOR (CD23) INHIBIT THE SPONTANEOUS MIGRATION OF U937 MONOCYTIC CELLS - NEUTRALIZATION OF MIF-ACTIVITY BY A **CD23 ANTIBODY.** FLORESROMO L; CAIRNS J A; MILLSUM M J; GORDON J (Reprint). UNIV BIRMINGHAM, SCH MED, DEPT IMMUNOL, W EXTENS, VINCENT DR, BIRMINGHAM B15 2TJ, W MIDLANDS, ENGLAND. IMMUNOLOGY (1989) Vol. 67, No. 4, pp. 547-549. Pub. country: ENGLAND. Language: ENGLISH.

L10 ANSWER 26 OF 27 MEDLINE on STN DUPLICATE 15
89052760. PubMed ID: 2847932. Interleukin 4 and soluble CD23 as progression factors for human B lymphocytes: analysis of their interactions with agonists of the phosphoinositide "dual pathway" of signalling. Gordon J; Cairns J A; Millsum M J; Gillis S; Guy G R. (Department of Immunology, University of Birmingham, GB. ) European journal of immunology, (1988 Oct) 18 (10) 1561-5. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.
AB Human B lymphocytes pre-activated for 24 h with a combination of phorbol dibutyrate [P(Bu)2] and ionomycin were found to provide excellent targets for assessing the detailed action of B cell progression factors. Both recombinant interleukin 4 (IL 4) and **affinity**-purified 25-kDa fragment of the CD23 molecule (sol-CD23) were shown to be active in this assay. While the progression activity of IL 4 was enhanced by continued co-culture with P(Bu)2, that of sol-CD23 was found to be more strictly dependent upon such a joint application with the phorbol ester. Similar requirements were observed for triggering cell-cycle progression in the pre-activated B cells when using a stimulating **CD23 antibody.** Ionomycin, in contrast to P(Bu)2, did not augment either IL 4 or sol-CD23 in these assays but did enhance significantly the progression activity of an anti-CDw40 antibody. When added to B cells concomitantly with, or prior to, a high dose of phorbol ester, IL 4 unexpectedly down-regulated the subsequent mitogenic response to this agent whereas, when added 24 h later, IL 4 up-regulated such stimulations. The latter sequence of additions resulted in a particularly dramatic induction of CD23 at the B cell surface, much more so than seen when B cells were incubated with either IL 4 alone or with IL 4 and P(Bu)2

together. This up-regulation of surface CD23 was, in turn, mirrored by the appearance of large amounts of the soluble form of the molecule in such cultures. The findings are discussed with reference to possible mechanisms through which IL 4 and CD23 interact to exert their multiple actions on B cell regulatory pathways.

L10 ANSWER 27 OF 27 MEDLINE on STN DUPLICATE 16
87317628. PubMed ID: 2957693. Coordinated action of IgE and a B-cell-stimulatory factor on the CD23 receptor molecule up-regulates B-lymphocyte growth. Guy G R; Gordon J. Proceedings of the National Academy of Sciences of the United States of America, (1987 Sep) 84 (17) 6239-43. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The CD23 (BLAST-2) antigen, recently identified as the low-**affinity** IgE receptor of B lymphocytes, has also been implicated as the focus for growth-promoting signals delivered to activated B cells by a low molecular weight B-cell growth factor (BCGF). Here we show that IgE and BCGF can coordinate B-lymphocyte growth through their opposing effects on the CD23 molecule. While the activation of purified quiescent B cells with phorbol 12-myristate 13-acetate led to the induction of 45-kDa CD23 at the surface membrane, the inclusion of IgE increased CD23 expression by a factor of approximately equal to 5. The addition of BCGF resulted in the rapid release of a 35-kDa form of CD23 from the cell surface. This shed molecule is associated with autocrine growth factor activity. Substantially more of this material was generated by BCGF acting on cells that had been stimulated in the presence of IgE. The combined effects of IgE and BCGF on DNA synthesis in activated B cells were more than additive. IgE similarly augmented the stimulatory capacity of a **CD23 antibody** that mimics the biological actions of BCGF. Binding of the anti-receptor antibody to its 45-kDa target at the B-cell surface also prompted the release of the 35-kDa soluble species. These results demonstrate a pleiotropy in the CD23 molecule with regard to both ligand binding and the subsequent behavior of the receptor. The ability of this single receptor to orchestrate a B-lymphocyte response through a variety of ligands and its role in normal and transformed autocrine growth are discussed.

=> s (bonnefoy j?/au or crowe j?/au or ellis j?/au or rapson n?/au or shearin j?/au)
L11 13452 (BONNEFOY J?/AU OR CROWE J?/AU OR ELLIS J?/AU OR RAPSON N?/AU OR SHEARIN J?/AU)

=> s l11 and CD23 antibody
L12 12 L11 AND CD23 ANTIBODY

=> dup remove l12
PROCESSING COMPLETED FOR L12
L13 7 DUP REMOVE L12 (5 DUPLICATES REMOVED)

=> d l13 1-7 cbib abs

L13 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
1999:736930 Document No. 131:350265 Antibodies to CD23. **Bonnefoy, Jean-Yves Marcel Paul**; Crowe, Scott James; **Ellis, Jonathan Henry**; **Rapson, Nicholas Timothy**; **Shearin, Jean** (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the preparation and characterization of murine monoclonal and humanized antibodies which bind to the CD23 (FcεRII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to CD23 with association rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these antibodies may find use in the treatment of autoimmune and inflammatory disorders.

L13 ANSWER 2 OF 7 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
1999:1848 Document No.: PREV199900001848. Binding of anti-CD23 monoclonal antibody to the leucine zipper motif of FcepsilonRII/CD23 on B cell membrane promotes its proteolytic cleavage. Evidence for an effect on the oligomer/monomer equilibrium. Munoz, Olivier; Brignone, Chrystelle; Grenier-Brossette, Nicole; **Bonnefoy, Jean-Yves**; Cousin, Jean-Louis [Reprint author]. INSERM U343, Hopital de l'Archet, B.P. 79, F-06202 Nice cedex 03, France. Journal of Biological Chemistry, (Nov. 27, 1998) Vol. 273, No. 48, pp. 31795-31800. print.
CODEN: JBCHA3. ISSN: 0021-9258. Language: English.
AB In the present study we have compared the binding of two monoclonal antibodies to CD23, EBVCS1 and mAb25, which recognize the stalk and the lectin domain, respectively, on the CD23 molecule. At 4degreeC, EBVCS1 binds to about 10% of the receptors recognized by mAb25 on the B cell surface. At 37degreeC, whereas mAb25 reaches its maximal binding within a few seconds, EBVCS1 requires 60 min to bind to the same extent. Stabilization of the oligomeric structure of CD23 with IgE strongly affects in a dose-dependent fashion the number of binding sites seen by EBVCS1 but not the t1/2 to reach them, suggesting that EBVCS1 binds to the coiled coil region through an allosteric mechanism. EBVCS1 rapidly down-modulates the membrane CD23 expression with a coincident increase of CD23-soluble fragments in the culture medium, an effect that is inhibited by IgE. In contrast, mAb25, as well as IgE, protects CD23 from proteolytic cleavage and stimulates its endocytosis. These results suggest that EBVCS1 unravels the coiled coil structure of CD23, rendering it more susceptible to proteolytic attack. This supports the oligomeric model proposed previously (Gould, H., Sutton, B., Edmeades, R., and Beavil, A. (1991) Monogr. Allergy 29, 28-49). The biological significance of these observations is discussed.

L13 ANSWER 3 OF 7 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
1999:124107 Document No.: PREV199900124107. CD23 modulates leukotriene-mediated broncho-constriction in a murine model of allergic asthma. Dasic, Gorana [Reprint author]; Juillard, Pierre [Reprint author]; Graber, Pierre [Reprint author]; Herren, Suzanne [Reprint author]; Angell, Tony; Knowles, Richard; **Bonnefoy, Jean-Yves**; Kosco-Vilbois, Marie H. [Reprint author]; Chvatchko, Yolande [Reprint author]. Geneva Biomed. Res. Inst., Glaxo Wellcome Res. and Dev. S.A., CH-1228 Plan-les-Ouates, Geneva, Switzerland. European Respiratory Journal, (Sept., 1998) Vol. 12, No. SUPPL. 28, pp. 193S. print.
Meeting Info.: European Respiratory Society Annual Congress. Geneva, Switzerland. September 19-23, 1998. The European Respiratory Society.
CODEN: ERJOEI. ISSN: 0903-1936. Language: English.

L13 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
1996:380155 Document No. 125:31943 Binding agents to CD23. **Bonnefoy, Jean-Yves Marcel Paul** (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.
AB Binding agents to CD23 useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized antibody or

fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23 antibody**, CD23-liposomes bind to CD14+ mononuclear cells and α chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal antibodies decrease CD23-liposome binding to activated blood monocytes, increases of monocyte nitrate production, oxidative burst and cytokine production by binding recombinant CD23 to CD11b and CD11c, etc.

L13 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 1
96071560. PubMed ID: 7585180. Marked amelioration of established collagen-induced arthritis by treatment with antibodies to CD23 in vivo. Plater-Zyberk C; **Bonnefoy J Y.** (Glaxo Institute for Molecular Biology, Immunology Department, Geneva, Switzerland. ) Nature medicine, (1995 Aug) 1 (8) 781-5. Journal code: 9502015. ISSN: 1078-8956. Pub. country: United States. Language: English.

AB CD23 is a low-affinity receptor for immunoglobulin E (IgE) expressed by a variety of haematopoietic cells. Proteolytic cleavage of the transmembrane receptor generates soluble forms, which can be detected in biological fluids. CD23 regulates many functional aspects of immune cells, both in its cell-associated and soluble forms. In view of the increased levels of CD23 in rheumatoid arthritis, we have studied the effect of neutralizing CD23 in type II collagen-induced arthritis in mice, a model for human rheumatoid arthritis. Successful disease modulation is achieved by treatment of arthritic DBA/1 mice with either polyclonal or monoclonal antibodies to mouse CD23. Treated mice show a dose-related amelioration of arthritis with significantly reduced clinical scores and number of affected paws. This improvement in clinical severity is confirmed by histological examination of the arthritic paws. A marked decrease in cellular infiltration of the synovial sublining layer and limited destruction of cartilage and bone is evident in animals treated with therapeutic doses of anti-**CD23 antibody.** These findings demonstrate the involvement of CD23 in a mouse model of human rheumatoid arthritis.

L13 ANSWER 6 OF 7 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
1995:521449 Document No.: PREV199598535749. Treatment with antibodies to CD23 markedly ameliorates an established collagen-induced arthritis in mice. Plater-Zyberk, Christine; **Bonnefoy, Jean-Yves.** Glaxo IMB, Immunol. Dep., 14 Chemin Des Aulx, CH-1228 Geneva, Switzerland. Arthritis and Rheumatism, (1995) Vol. 38, No. 9 SUPPL., pp. S310.
Meeting Info.: 59th National Scientific Meeting of the American College of Rheumatology and the 30th National Scientific Meeting of the Association of Rheumatology Health Professionals. San Francisco, California, USA. October 21-26, 1995.
CODEN: ARHEAW. ISSN: 0004-3591. Language: English.

L13 ANSWER 7 OF 7 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 2
91:364397 The Genuine Article (R) Number: FT273. IGE AND SWITCHING PHENOMENA. **BONNEFOY J Y (Reprint).** GLAXO INST MOLEC BIOL, CHEMIN AULX, CH-1228 PLAN LES OUATES, SWITZERLAND (Reprint). SEMAINE DES HOPITAUX (1991 ) Vol. 67, No. 26-2, pp. 1199-1200. Pub. country: SWITZERLAND. Language: French.
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB In allergic disorders, IgE increases following allergen stimulation. In vitro IgE synthesis is the result of a complex interaction between T-cells, B-cells and monocytes, controlled by cytokines produced by T-cells and monocytes (IL-4, IL-5, IFN-gamma, and IL-6). IL-4 acts as a switching factor to induce synthesis of IgE. IFN-gamma inhibits IL-4 induced IgE synthesis. IL-4 is a mastocyte growth factor, as well as IL-3. Moreover, IL-4 is a potent inducer of FceR/CD23 expression of B-cells and monocytes. Monoclonal anti-**CD23 antibodies** inhibit IL-4-induced IgE synthesis in an isotype-specific manner. IL-4-producing T-cells also produce IL-5 which induces differentiation of